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TITLE

SEARCH REQ

Requester's Full Name: Kristin Dinacchi Date: 9/5/08  
 Alt Unit: 1626 Phone Number: 805232 Serial Number: 10/569486  
 Location (Bldg/Room): 234 Mailbox #: N/A Results Format Preferred (circle): PAPER (DISK)

To ensure an efficient and quality search, please attach a copy of the cover sheet, abstract, and abstract or fill out the following:

Title of Invention: Process for Producing an economic vasodilated response

Inventors (please provide full names):

Weigi Wang & Tetuya Ikemoto

Earliest Priority Date: 08/23/03

#### Search Topic:

Please provide a detailed statement of the search topic, and then also as specifically as possible the subject matter to be searched. Include the desired species or structures, keywords, synonyms, acronyms, and registry numbers, and symbols with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if known.

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Please search claim 1.

=> file registry

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DICTIONARY FILE UPDATES: 7 SEP 2008 HIGHEST RN 1047406-12-1

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FILE COVERS 1907 - 8 Sep 2008 VOL 149 ISS 11  
FILE LAST UPDATED: 7 Sep 2008 (20080907/ED)

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'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d stat que L25

L23 30349 SEA FILE=CAPLUS ABB=ON PLU=ON WANG W?/AU  
L24 645 SEA FILE=CAPLUS ABB=ON PLU=ON IKEMOTO T?/AU  
L25 8 SEA FILE=CAPLUS ABB=ON PLU=ON L23 AND L24

=> file medline embase biosis wpix

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=> d stat que L26

L23 30349 SEA FILE=CAPLUS ABB=ON PLU=ON WANG W?/AU  
L24 645 SEA FILE=CAPLUS ABB=ON PLU=ON IKEMOTO T?/AU  
L25 8 SEA FILE=CAPLUS ABB=ON PLU=ON L23 AND L24  
L26 9 SEA L25

=> dup rem L25 L26

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PROCESSING COMPLETED FOR L26

L45 10 DUP REM L25 L26 (7 DUPLICATES REMOVED)  
ANSWERS '1-8' FROM FILE CAPLUS  
ANSWERS '9-10' FROM FILE WPIX

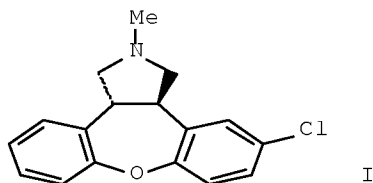
=> d ibib abs L45 1-8; d iall L45 9-10

L45 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1  
ACCESSION NUMBER: 2007:461305 CAPLUS Full-text  
DOCUMENT NUMBER: 146:462239  
TITLE: Process for preparation of dibenzoxepinopyrrole  
compounds and intermediates  
INVENTOR(S): Wang, Weiqi; Ikemoto, Tetsuya  
PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan  
SOURCE: PCT Int. Appl., 33pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2007046554	A1	20070426	WO 2006-JP321452	20061020
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,			

10/569486

KG, KZ, MD, RU, TJ, TM  
JP 2007137877 A 20070607 JP 2006-286275 20061020  
PRIORITY APPLN. INFO.: JP 2005-307588 A 20051021  
OTHER SOURCE(S): CASREACT 146:462239; MARPAT 146:462239  
GI



AB Disclosed is a process for preparation of compound I and a pharmaceutically acceptable salt thereof in a multi-step synthesis, which comprises intramol. cyclization and reduction Also disclosed is intermediates for the production of the compound I. Further disclosed is a process for production of the intermediates.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2006:787645 CAPLUS Full-text

DOCUMENT NUMBER: 145:230397

TITLE: Preparation of unsaturated (hetero)aromatic compounds having electron-withdrawing group

INVENTOR(S): Wang, Wei-Chi; Ikemoto, Tetsuya

PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 14pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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JP 2006206466	A	20060810	JP 2005-17794	20050126
PRIORITY APPLN. INFO.:			JP 2005-17794	20050126
OTHER SOURCE(S):	MARPAT 145:230397			

AB ArCH:CRY [Ar = (un)substituted (hetero)aryl; R = C1-12 linear or branched alkyl; aryl-C1-8 alkyl; Y = electron-withdrawing group], useful as intermediates for drugs and agrochems., are prepared by reacting ArH (Ar = same as above) with ZC:CRY (R, Y = same as above; Z = lower alkoxy) or Z2CCRY (R, Y = same as above; Z = lower alkoxy) in the presence of acids or compds. capable of mineral acids upon hydrolysis. Thus, an AcOH solution of 1,3,5-(MeO)3C6H3 was treated with (MeO)2CHCHBuCO2Et and an aqueous HBr solution under stirring at room temperature overnight to give 67.0% 2,4,6-(MeO)3C6H2CH:CBuCO2Et.

L45 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3

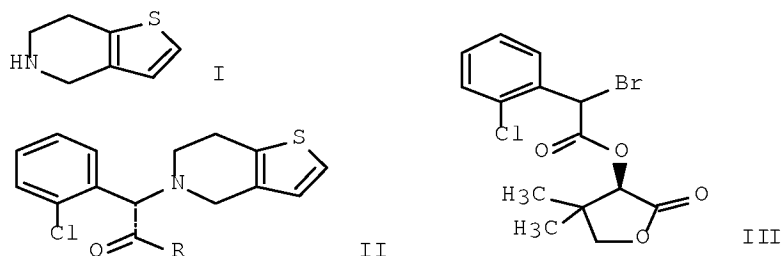
ACCESSION NUMBER: 2006:468875 CAPLUS Full-text

DOCUMENT NUMBER: 144:488633

10/569486

TITLE: Preparation of antithrombotic clopidogrel  
 INVENTOR(S): Wang, Wei-Chi; Ikemoto, Tetsuya; Liang, Ting  
 PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006124326	A	20060518	JP 2004-314850	20041028
PRIORITY APPLN. INFO.:			JP 2004-314850	20041028
OTHER SOURCE(S):	MARPAT 144:488633			
GI				



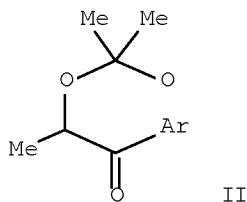
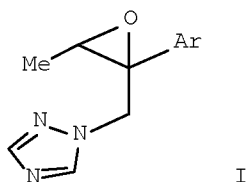
AB Clopidogrel or its pharmaceutically-acceptable salts are prepared by reacting 2-ClC<sub>6</sub>H<sub>4</sub>CHXCOR [X = halo, OSO<sub>2</sub>R<sub>1</sub>; R<sub>1</sub> = lower (halo)alkyl, (un)substituted aryl; R = substituent containing asym. C] with 4,5,6,7-tetrahydrothieno[3,2-c]pyridine (I) and converting the resulting II (R = same as above). Thus, SOCl<sub>2</sub> was added dropwise to a toluene solution of 40 g  $\alpha$ -bromo-(2-chlorophenyl)acetic acid at room temperature and the reaction mixture was heated at 75° for 3 h. The toluene solution of the resulting acid chloride was added to a THF solution of 24.5 g D-(-)-pantoyl lactone and Et<sub>3</sub>N at 0-5° and the reaction mixture was stirred for 1 h to give 39.4 g (R)-4,4-dimethyl-2-oxotetrahydrofuran-3-yl  $\alpha$ -bromo-(2-chlorophenyl)acetate (III). A THF solution of 3.26 g I was added dropwise to a THF solution of III, Et<sub>3</sub>N, and Bu<sub>4</sub>NI at 0-5° and the reaction mixture was stirred for 1 h to give 67% (R)-4,4-dimethyl-2-oxotetrahydrofuran-3-yl (S)- $\alpha$ -5-(4,5,6,7-tetrahydro[3,2-c]thienopyridyl)-2-chlorophenylacetate. This was treated with a mixture of LiOMe, MeOH, and Me<sub>3</sub>COMe at 0° for 4 h to give 57% clopidogrel.

L45 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 4  
 ACCESSION NUMBER: 2005:490343 CAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 143:43877  
 TITLE: Process for producing epoxytriazole compounds and intermediate therefor  
 INVENTOR(S): Wang, Weiqi; Ikemoto, Tetsuya  
 PATENT ASSIGNEE(S): Sumitomo Chemical Company, Limited, Japan

10/569486

SOURCE: PCT Int. Appl., 61 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051879	A1	20050609	WO 2004-JP17992	20041126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2005154377	A	20050616	JP 2003-398252	20031127
EP 1693358	A1	20060823	EP 2004-819487	20041126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1906146	A	20070131	CN 2004-80040853	20041126
CN 101250163	A	20080827	CN 2008-10081772	20041126
IN 2006CN02344	A	20070706	IN 2006-CN2344	20060626
PRIORITY APPLN. INFO.:			JP 2003-398252	A 20031127
			CN 2004-80040853	A3 20041126
			WO 2004-JP17992	W 20041126
OTHER SOURCE(S):			MARPAT 143:43877	
GI				



AB Process for the preparation of compound I [Ar = difluorophenyl] from compound II [Ar has the same meaning as defined above.] was provided. For example, a

solution of (2R,3R)-3-(2',4'-difluorophenyl)-3,4-ethoxy-2-(1'-methoxy-1'-methylethoxy)butane (34.0 g) in toluene (60 mL), methanol (10 mL) and water (5 mL) was treated with methanesulfonic acid (56 mg) at room temperature for 5 min. Aqueous work-up afforded (2R,3R)-3-(2',4'-difluorophenyl)-2-hydroxy-3,4-epoxybutane (III) (24.5 g). Then, exposure of a mixture of III (24.5 g) in toluene (108 mL) to methanesulfonyl chloride (14.6 g) and triethylamine (13.5 g) at 0-15 °C gave (2R,3R)-3-(2',4'-difluorophenyl)-3,4-epoxy-2-methanesulfonyloxybutane (IV) (32.3 g). To a mixture of IV in DMF (35 mL) was added 1,2,4-triazole sodium salt, e.g., in-situ prepared from 1,2,4-triazole (10.4 g) and NaH (5.56 g, 60% in paraffin), over a period of 2 h maintaining 55-65 °C, the resulting mixture was stirred for addnl. 2 h to furnish compound (2R,3S)-I [Ar = 2,4-difluorophenyl] (13.4 g). Of note, compound I is an useful intermediate for a fungicide.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2005:487859 CAPLUS Full-text

DOCUMENT NUMBER: 143:26493

TITLE: Preparation of syn-1,3-diols by stereoselective reduction

INVENTOR(S): Wang, Wei-Chi; Ikemoto, Tetsuya

PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 22 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

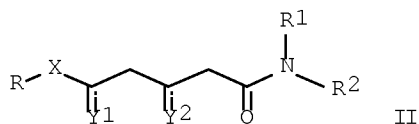
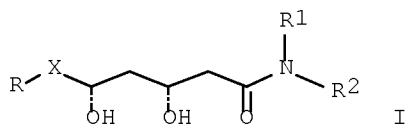
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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JP 2005145833	A	20050609	JP 2003-381816	20031111
PRIORITY APPLN. INFO.:			JP 2003-381816	20031111

GI



AB Title compds. I [X = CH:CH, CH<sub>2</sub>CH<sub>2</sub>, OCH<sub>2</sub>; R = aromatic group having inert group; R<sub>1</sub>, R<sub>2</sub> = lower alkyl; NR<sub>1</sub>R<sub>2</sub> may form (O-containing) nonarom. heterocyclyl], useful as hypolipemic agents (no data), are prepared by (A) mixing R<sub>3</sub>BOR<sub>4</sub> (R<sub>3</sub> = lower alkyl; R<sub>4</sub> = lower alkyl, aryl) or R<sub>5</sub>B with NaBH<sub>4</sub>

in lower alc.-THF mixed solvent system and (B) reduction of keto alcs. II (Y1 or Y2 = O; the other = OH; the broken line may be bond; X, R, R1, R2 = same as above) with the mixts. Preparation of (cyclization products of) carboxylic acids (salts) corresponding to the products is also claimed. Thus, THF-MeOH solution of 7-[3-(4-fluorophenyl)-1-isopropyl-1H-indol-2-yl]-5-hydroxy-3-oxo-hept-6E-enoic acid dimethylamide was added to THF-MeOH solution containing NaBH4 and Et2BOMe at -78° over 35 min and the reaction mixture was stirred for 2.5 h to give the corresponding syn-1,3-diol with 79.4% yield.

L45 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2005:378843 CAPLUS Full-text

DOCUMENT NUMBER: 143:78029

TITLE: A practical synthesis of 3-indolyl  
 $\alpha,\beta$ -unsaturated carbonyl compounds

AUTHOR(S): Wang, Weiqi; Ikemoto, Tetsuya

CORPORATE SOURCE: Fine Chemicals Research Laboratory, Ltd., Sumitomo  
Chemical Co., Nishiyodogawa-ku, Osaka, 555-0021, Japan

SOURCE: Tetrahedron Letters (2005), 46(22), 3875-3878

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:78029

AB An acid-catalyzed practical synthesis of 3-indolyl  $\alpha,\beta$ -unsatd. carbonyl compds. using Me 3-methoxyacrylate, Me 3,3-dimethoxypropionate, or 1,1-dimethoxy-3-butanone is reported. HCl aqueous solution (35%) catalyzes this reaction efficiently in acetic acid. One of the most favorable substrates is 3-(4-fluorophenyl)-1-isopropyl-1H-indole, which reacts nearly quant. to give the corresponding  $\alpha,\beta$ -unsatd. ester, and the scope of the reaction can be extended to some electron-rich benzene derivs.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 2003:1007919 CAPLUS Full-text

DOCUMENT NUMBER: 140:59645

TITLE: Production methods of epoxytriazole derivative and  
intermediate therefor

INVENTOR(S): Wang, Weiqi; Ikemoto, Tetsuya

PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan; Sumitomo  
Chemical Company, Limited

SOURCE: U.S. Pat. Appl. Publ., 13 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

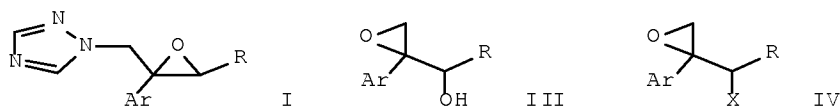
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 20030236419	A1	20031225	US 2002-335400	20021231
US 6884892	B2	20050426		
CA 2489611	A1	20031231	CA 2003-2489611	20030610
WO 2004000826	A1	20031231	WO 2003-JP7316	20030610
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,				
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH,				



PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 AU 2003242144 A1 20040106 AU 2003-242144 20030610  
 EP 1535914 A1 20050601 EP 2003-730869 20030610  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 CN 1662518 A 20050831 CN 2003-814450 20030610  
 CN 1970522 A 20070530 CN 2006-10169394 20030610  
 US 20040267024 A1 20041230 US 2004-842600 20040510  
 US 7297802 B2 20071120  
 IN 2004CN03158 A 20060303 IN 2004-CN3158 20041213  
 PRIORITY APPLN. INFO.: JP 2002-180610 A 20020620  
 JP 2002-313317 A 20021028  
 JP 2002-318833 A 20021031  
 US 2002-335400 A3 20021231  
 CN 2003-814450 A3 20030610  
 WO 2003-JP7316 W 20030610

OTHER SOURCE(S): MARPAT 140:59645  
 GI



AB An epoxytriazole derivative (I) [wherein Ar is a Ph group optionally substituted by 1 to 3 halogen atom(s) or trifluoromethyl group, R is a hydrogen atom or lower alkyl group] useful as an intermediate for anti-fungal agents and an intermediate therefor having high quality can be produced economically and efficiently by the following industrial means. A compound of the following formula  $\text{ArCOCH(R)OH}$  (II) (Ar, R = same as above) is reacted with trimethyloxosulfonium salt and the like in the presence of a base to give an epoxide compound (III; Ar, R = same as above) which is converted to the compound (IV; Ar, R = same as above; X is a leaving group) and then reacted with 1,2,4-triazole in the presence of a base. Thus, trimethyloxosulfonium bromide (2.66 g) was dissolved in DMSO (13 mL) and treated with sodium hydride (60 % dispersion in oil, 0.27 g) by small portions at room temperature and then after generation of hydrogen stopped, a solution (5 mL) of (2R)-2',4'-difluoro-2-hydroxypropiophenone (V) (1.10 g) in DMSO slowly and the mixture was stirred for about 30 min to give, after workup, a 12:1 mixture (1.06 g) of (2R,3R)-3-(2',4'-difluorophenyl)-3,4-epoxy-2-butanol and its (2R,3S)-diastereomer. The latter diastereomer mixture (0.3 g) and 0.312 mL  $\text{Et}_3\text{N}$  were added to toluene (5 mL), cooled to 0-10°, treated dropwise with methanesulfonyl chloride (0.14 mL), and stirred for 1 h to give, after workup, 0.42 g (2R,3R)-3-(2',4'-difluorophenyl)-3,4-epoxy-2-methanesulfonyloxybutane (VI). To a solution (3 mL) of 1,2,4-triazole (0.259 g) in DMF was added small portions of NaH (60% dispersion in oil, 0.12 g) at .apprx.20° and red for about 3 h until hydrogen was not generated, to give a solution of sodium salt of 1,2,4-triazole thus obtained which was treated dropwise with a solution (5.5 mL) of the total amount of VI obtained above in DMF at room temperature

and stirred at 75–80° for 1.5 h to give, after workup and silica gel chromatog., 0.185 g (2S,3R)-2-(2,4-difluorophenyl)-3-methyl-2-[(1H-1,2,4-triazol-1-yl)methyl]oxirane (44% yield). The reaction of the compound II (not protected) with trimethyloxosulfonium salt and the like surprisingly proceeded easily to give compound III. When compound II was in an optically active form, e.g. V, induction of racemization in this reaction was worried, but racemization was not observed in most cases. The use of compound II resulted in strikingly improved diastereoselectivity as compared to the use of a compound protected by tetrahydropyranyl group. Moreover, the epoxytriazole derivative I could be synthesized efficiently from the compound IV, which was produced by substituting the hydroxy group in compound III for a leaving group.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2008:806468 CAPLUS Full-text  
 DOCUMENT NUMBER: 149:104674  
 TITLE: Process for producing intermediate of asenapine synthesis  
 INVENTOR(S): Tokuda, Osamu; Wang, Weiqi; Ikemoto, Tetsuya  
 PATENT ASSIGNEE(S): Sumitomo Chemical Company, Limited, Japan  
 SOURCE: PCT Int. Appl., 17pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008078482	A1	20080703	WO 2007-JP72601	20071115
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

JP 2008174547 A 20080731 JP 2007-313406 20071204

PRIORITY APPLN. INFO.: JP 2006-346735 A 20061222

AB Disclosed is a process for producing 2-(2-(4-chlorophenoxy)phenyl)acetic acid by reaction of (2-chlorophenyl)acetic acid with 4-chlorophenol. Thus, a mixture of (2-chlorophenyl)acetic acid (1.00 g), 4-chlorophenol (0.78 g), Cs<sub>2</sub>CO<sub>3</sub> (3.80 g) and CuBr (42 mg) in diethyleneglycol di-Me ether (5 mL) was stirred at 145° for 8 h. After cooling and adjusting pH using HCl, the resulting reaction mixture was extracted with toluene. The organic layer was washed with brine, dried over MgSO<sub>4</sub> and filtered to give a solution of 2-(2-(4-chlorophenoxy)phenyl)acetic acid in toluene (59% yield).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/569486

L45 ANSWER 9 OF 10 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN  
 ACCESSION NUMBER: 2005-233057 [24] WPIX Full-text  
 DOC. NO. CPI: C2005-073858 [24]  
 TITLE: Synthesis of aromatic unsaturated compound useful as  
 synthetic intermediate in pharmaceuticals, involves  
 reacting specific aromatic compound with unsaturated  
 compound in presence of compound producing mineral acid  
 on hydrolysis  
 DERWENT CLASS: B05; C03  
 INVENTOR: IKEMOTO T; O I; WANG W; WENG W  
 PATENT ASSIGNEE: (SUMO-C) SUMITOMO CHEM CO LTD  
 COUNTRY COUNT: 107

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005021465	A1	20050310	(200524)*	JA	35[0]	
JP 2005097227	A	20050414	(200527)	JA	18	
EP 1666440	A1	20060607	(200638)	EN		
CN 1871188	A	20061129	(200720)	ZH		
KR 2007000387	A	20070102	(200755)	KO		
IN 2006CN01042	P4	20070629	(200768)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005021465	A1	WO 2004-JP12601	20040825
JP 2005097227	A	JP 2003-384566	20031114
CN 1871188	A	CN 2004-80030885	20040825
EP 1666440	A1	EP 2004-772557	20040825
EP 1666440	A1	WO 2004-JP12601	20040825
KR 2007000387	A	WO 2004-JP12601	20040825
IN 2006CN01042	P4	WO 2004-JP12601	20040825
KR 2007000387	A	KR 2006-703787	20060224
IN 2006CN01042	P4	IN 2006-CN1042	20060327

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1666440	A1 Based on	WO 2005021465 A
KR 2007000387	A Based on	WO 2005021465 A

PRIORITY APPLN. INFO: JP 2003-384566 20031114  
 JP 2003-209042 20030827

INT. PATENT CLASSIF.:

MAIN: C07B037-04  
 IPC ORIGINAL: C07B0037-00 [I,C]; C07B0037-00 [I,C]; C07B0037-04 [I,A];  
 C07C0067-00 [I,C]; C07C0067-00 [I,C]; C07C0067-343 [I,A];  
 C07C0067-343 [I,A]; C07C0069-00 [I,C]; C07C0069-734 [I,A];  
 ; C07D0209-10 [I,A]; C07D0209-24 [I,A]  
 IPC RECLASSIF.: C07B0037-00 [I,C]; C07B0037-04 [I,A]; C07B0061-00 [I,A];  
 C07B0061-00 [I,C]; C07C0067-00 [I,C]; C07C0067-32 [I,A];  
 C07C0067-343 [I,A]; C07C0069-00 [I,C]; C07C0069-736 [I,A];  
 ; C07D0209-00 [I,C]; C07D0209-08 [I,A]; C07D0209-10 [I,A];  
 ; C07D0209-12 [I,A]; C07D0209-18 [I,A]; C07D0209-24 [I,A]

ECLA: C07B0037-04; C07C0067-343+69/734; C07D0209-08;  
 C07D0209-10; C07D0209-12; C07D0209-18; C07D0209-24

10/569486

BASIC ABSTRACT:

WO 2005021465 A1 UPAB: 20071024

NOVELTY - Aromatic compound (1) is reacted with unsaturated compound (2) or (3) in presence of acid or compound producing a mineral acid on hydrolysis, to obtain aromatic unsaturated compound (4).

DETAILED DESCRIPTION - The synthesis of aromatic unsaturated compound of formula (4) involves reacting aromatic compound of formula (1) with unsaturated compound of formula (2) or (3) in presence of acid or a compound producing mineral acid on hydrolysis.

Ar = optionally substituted aromatic/hetero aromatic;

Y = electron attractive group; and

Z = lower alkoxy.

USE - As synthetic intermediate in pharmaceuticals and agrochemicals.

ADVANTAGE - The method enables effective synthesis of aromatic unsaturated compound. The method is simple, economical, eco-friendly in nature and has high industrial utility. MANUAL CODE: CPI: B06-D01; B06-H; B07-H; B10-J02; C06-D01; C06-H;

C07-H; C10-J02

L45 ANSWER 10 OF 10 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN  
ACCESSION NUMBER: 2005-074259 [08] WPIX Full-text  
CROSS REFERENCE: 2004-120199  
DOC. NO. CPI: C2005-025302 [08]  
TITLE: Preparation of epoxy derivative, for preparation of epoxytriazole derivative useful synthetic intermediate for anti-fungal agents, involves reacting aryl derivative with trimethyloxosulfonium or trimethylsulfonium salt in presence of base  
DERWENT CLASS: B03; C02  
INVENTOR: IKEMOTO T; WANG W  
PATENT ASSIGNEE: (SUMO-C) SUMIKA FINE CHEM CO LTD; (SUMO-C) SUMITOMO CHEM CO LTD  
COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20040267024	A1	20041230	(200508)*	EN	13[0]	
US 7297802	B2	20071120	(200778)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20040267024	A1 Div Ex	US 2002-335400	20021231
US 20040267024	A1	US 2004-842600	20040510
US 7297802	B2 Div Ex	US 2002-335400	20021231
US 7297802	B2	US 2004-842600	20040510

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 7297802	B2 Div ex	US 6884892 B

PRIORITY APPLN. INFO: JP 2002-318833 20021031  
JP 2002-180610 20020620  
JP 2002-313317 20021028

INT. PATENT CLASSIF.:

10/569486

IPC ORIGINAL: C07D0303-00 [I,A]; C07D0303-00 [I,C]  
IPC RECLASSIF.: C07D0257-00 [I,C]; C07D0257-02 [I,A]; C07D0405-00 [I,C];  
C07D0405-06 [I,A]  
ECLA: C07D0405-06  
USCLASS NCLM: 548/252.000  
BASIC ABSTRACT:

US 20040267024 A1 UPAB: 20050707

NOVELTY - Preparation of epoxy derivative involves reacting aryl derivative with a trimethyloxosulfonium salt or a trimethylsulfonium salt in the presence of a base.

DETAILED DESCRIPTION - Preparation of epoxy derivative of formula (II) involves reacting aryl derivative of formula  $\text{Ar}-\text{C}(\text{O})-\text{C}(\text{R})-\text{OH}$  (I) with a trimethyloxosulfonium salt or a trimethylsulfonium salt in the presence of a base.

Ar = phenyl (optionally mono- - tri-substituted by halo or trifluoromethyl) (preferably 2,4-difluorophenyl);

R = H or lower alkyl (preferably methyl).

INDEPENDENT CLAIMS are included for the following:

(1) preparation of aryltriazole derivative of formula (III) or its salt involving preparing (II) and reacting with 1,2,4-triazole in the presence of base;

(2) preparation of epoxyaryl derivative of formula (IV) involving preparing (II) and converting to (IV);

(3) intermediate (2R)-2-(1-Ethoxyethoxy)-1-(2,4-difluorophenyl)-1-propanone.

X = leaving group.

USE - For preparation of epoxytriazole derivative e.g. 1-(2-(2,4-difluoro-phenyl)-3-methyl-oxiranylmethyl)-1H-(1,2,4)triazole, useful synthetic intermediate for anti-fungal agents such as triazole compounds.

ADVANTAGE - The epoxytriazole derivative, useful synthetic intermediate for anti-fungal agents having high quality can be produced economically and efficiently industrially. The epoxidation proceeds even without protecting deprotected 1-(2,4-difluoro-phenyl)-2-(tetrahydro- pyran-2-yloxy)-propan-1-one. The diastereoselectivity is dramatically improved.

MANUAL CODE: CPI: B07-A03; B07-D13; C07-A03; C07-D13

=> file casreact

FILE 'CASREACT' ENTERED AT 14:11:16 ON 08 SEP 2008

USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

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FILE CONTENT:1840 - 31 Aug 2008 VOL 149 ISS 10

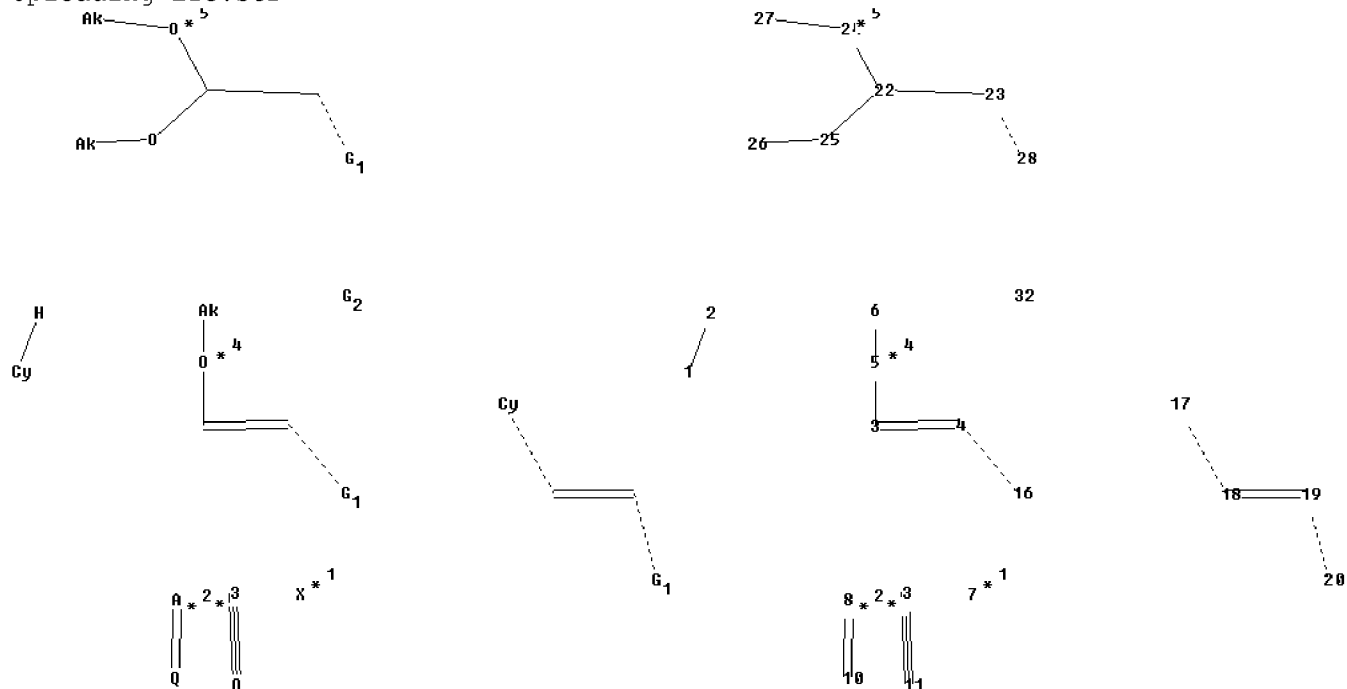
New CAS Information Use Policies, enter HELP USAGETERMS for details.

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*      CASREACT now has more than 15.3 million reactions      *
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CASREACT contains reactions from CAS and from: ZIC/VINITI database (1974-1999) provided by InfoChem; INPI data prior to 1986; Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich; organic reactions, portions copyright 1996-2006 John Wiley & Sons, Ltd., John Wiley and Sons, Inc., Organic Reactions Inc., and Organic Syntheses Inc. Reproduced under license. All Rights Reserved.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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chain nodes :

10/569486

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1  2  3  4  5  6  7 16 17 18 19 20 22 23 24 25 26 27 28 32
ring/chain nodes :
8  9 10 11
chain bonds :
1-2  3-4  3-5  4-16  5-6  17-18  18-19  19-20  22-23  22-24  22-25  23-28  24-27
25-26
ring/chain bonds :
8-10  9-11
exact/norm bonds :
1-2  3-5  4-16  5-6  8-10  9-11  17-18  19-20  22-24  22-25  23-28  24-27  25-26

exact bonds :
3-4  18-19  22-23
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G1:[\*1],[\*2],[\*3]

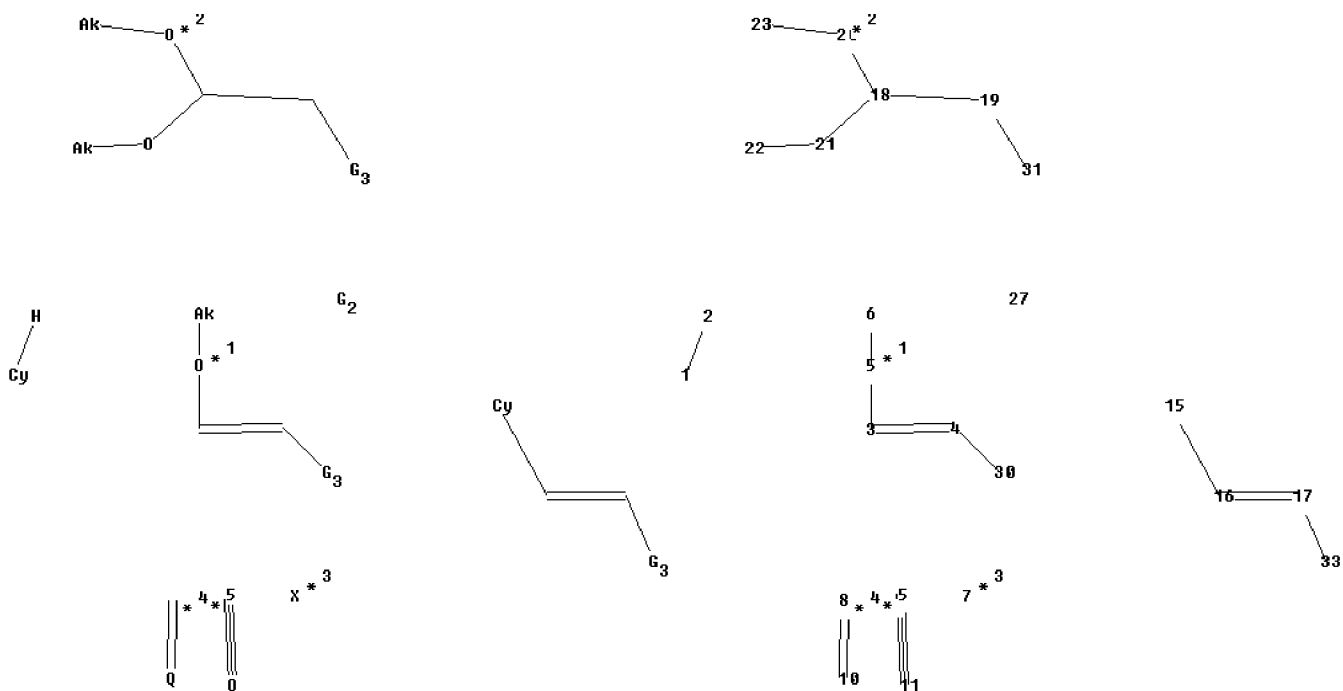
G2:[\*4],[\*5]

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10:CLASS
11:CLASS 16:CLASS 17:Atom 18:CLASS 19:CLASS 20:CLASS 22:CLASS 23:CLASS
24:CLASS 25:CLASS
26:CLASS 27:CLASS 28:CLASS 32:CLASS
Generic attributes :
1:
Saturation          : Unsaturated
17:
Saturation          : Unsaturated
```

```
fragments assigned reactant role:
containing 1
containing 32
fragments assigned product role:
containing 17
reaction site bonds:
17-18:CC
```

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10/569486



chain nodes :

1 2 3 4 5 6 7 8 9 10 11 15 16 17 18 19 20 21 22 23 27 30 31  
33

chain bonds :

1-2 3-4 3-5 4-30 5-6 8-10 9-11 15-16 16-17 17-33 18-19 18-20 18-21 19-31  
20-23 21-22

exact/norm bonds :

1-2 3-5 4-30 5-6 8-10 9-11 15-16 17-33 18-20 18-21 19-31 20-23 21-22

exact bonds :

3-4 16-17 18-19

G2:[\*1],[\*2]

G3:[\*3],[\*4],[\*5]

Hydrogen count :

3:= exact 1 4:= exact 1 16:= exact 1 17:= exact 1 18:= exact 1 19:= exact 2

Connectivity :

3:2 E exact RC ring/chain 4:2 E exact RC ring/chain 16:2 E exact RC ring/chain  
17:2 E exact RC ring/chain 18:3 E exact RC ring/chain 19:2 E exact RC ring/chain

Match level :

1:Atom 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS  
10:CLASS  
11:CLASS 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS  
22:CLASS 23:CLASS  
27:CLASS 30:CLASS 31:CLASS 33:CLASS

Generic attributes :

1:  
Saturation : Unsaturated  
15:  
Saturation : Unsaturated



10/569486

fragments assigned reactant role:  
containing 1  
containing 27  
fragments assigned product role:  
containing 15  
reaction site bonds:  
15-16:CC

=> d stat que L14  
L1 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.  
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L3 SCR 278 OR 1342  
L4 143 SEA FILE=CASREACT SUB=L2 SSS FUL L1 AND L3 ( 742 REACTIONS)  
L5 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.  
L7 43 SEA FILE=CASREACT SUB=L4 SSS FUL L5 ( 207 REACTIONS)  
L8 TRANSFER PLU=ON L4 1- RX : 1312 TERMS  
L9 1312 SEA FILE=REGISTRY ABB=ON PLU=ON L8/RN  
L10 441 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND X/ELS  
L11 421 SEA FILE=REGISTRY ABB=ON PLU=ON L10 AND C/ELS  
L12 20 SEA FILE=REGISTRY ABB=ON PLU=ON L10 NOT L11  
L13 188275 SEA FILE=CASREACT ABB=ON PLU=ON L12  
L14 24 SEA FILE=CASREACT ABB=ON PLU=ON L13 (L) L7

=> d stat que L40  
L1 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.  
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L3 SCR 278 OR 1342  
L4 143 SEA FILE=CASREACT SUB=L2 SSS FUL L1 AND L3 ( 742 REACTIONS)  
L5 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.  
L7 43 SEA FILE=CASREACT SUB=L4 SSS FUL L5 ( 207 REACTIONS)  
L8 TRANSFER PLU=ON L4 1- RX : 1312 TERMS  
L9 1312 SEA FILE=REGISTRY ABB=ON PLU=ON L8/RN  
L10 441 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND X/ELS  
L11 421 SEA FILE=REGISTRY ABB=ON PLU=ON L10 AND C/ELS  
L12 20 SEA FILE=REGISTRY ABB=ON PLU=ON L10 NOT L11  
L13 188275 SEA FILE=CASREACT ABB=ON PLU=ON L12  
L14 24 SEA FILE=CASREACT ABB=ON PLU=ON L13 (L) L7  
L37 75833 SEA FILE=CASREACT ABB=ON PLU=ON 64-19-7  
L40 2 SEA FILE=CASREACT ABB=ON PLU=ON L37 (L) L14

=> d stat que L21  
L1 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

L2 ( 190274)SEA FILE=CASREACT ABB=ON PLU=ON ACYCLIC ALKENE/FG.PRO  
L3 SCR 278 OR 1342  
L4 143 SEA FILE=CASREACT SUB=L2 SSS FUL L1 AND L3 ( 742 REACTIONS)  
L5 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

L7 43 SEA FILE=CASREACT SUB=L4 SSS FUL L5 ( 207 REACTIONS)  
L8 TRANSFER PLU=ON L4 1- RX : 1312 TERMS  
L9 1312 SEA FILE=REGISTRY ABB=ON PLU=ON L8/RN  
L10 441 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND X/ELS  
L11 421 SEA FILE=REGISTRY ABB=ON PLU=ON L10 AND C/ELS  
L12 20 SEA FILE=REGISTRY ABB=ON PLU=ON L10 NOT L11  
L13 188275 SEA FILE=CASREACT ABB=ON PLU=ON L12  
L14 24 SEA FILE=CASREACT ABB=ON PLU=ON L13 (L) L7  
L16 11 SEA FILE=REGISTRY ABB=ON PLU=ON L12 AND M/ELS  
L17 9 SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L16  
L18 153759 SEA FILE=CASREACT ABB=ON PLU=ON L17  
L19 31 SEA FILE=CASREACT ABB=ON PLU=ON L18 (L) L4  
L21 15 SEA FILE=CASREACT ABB=ON PLU=ON L19 AND L14

=> s L14 or L40 or L21  
L46 24 L14 OR L40 OR L21

=> d ibib abs hit L46 1-24

L46 ANSWER 1 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 148:262034 CASREACT Full-text

TITLE: Synthesis and structure of polyunsaturated  
[10]paracyclophane annulated by two azulene rings

AUTHOR(S): Kuroda, Shigeyasu; Obata, Yuji; Thanh, Nguyen Chung;  
Miyatake, Ryuta; Horino, Yoshikazu; Oda, Mitsunori

CORPORATE SOURCE: Department of Applied Chemistry, Graduate School of  
Science and Engineering, University of Toyama, Toyama,  
930-8555, Japan

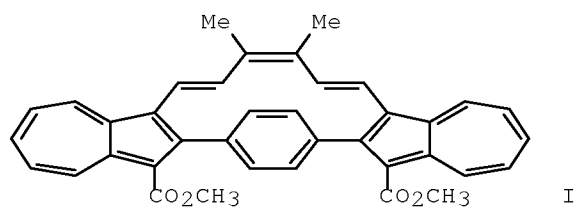
SOURCE: Tetrahedron Letters (2008), 49(3), 552-556  
CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

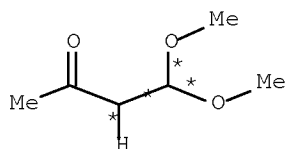
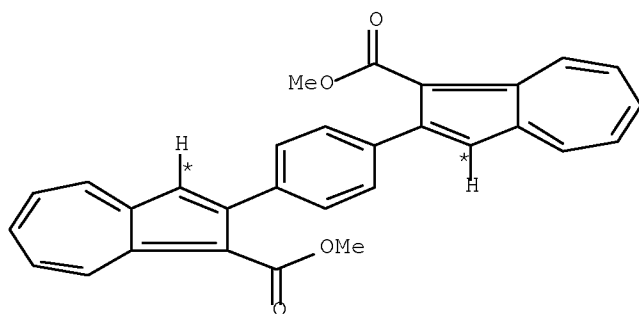
GI



AB The polyunsatd. [10]cyclophane I was synthesized from 1,4-diacetylbenzene by a four-step sequence involving the modified Yasunami azulene synthesis, introduction of two butenone units, and a subsequent McMurry coupling reaction. The crystal structures of I and a synthetic intermediate were determined by X-ray crystallog. anal. The results revealed that (1) the benzene ring of I is distorted as a boat form with relatively small bending angles and (2) the azulene rings of the intermediate show large out-of-plane deformation along the short azulene mol. axis.

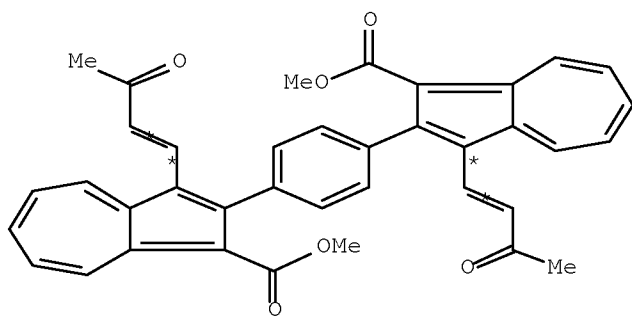
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(2) →

10/569486



F  
YIELD 28%

RX(2) RCT C 1006389-39-4, E 5436-21-5

STAGE(1)

RGT G 16872-11-0 HBF4

STAGE(2)

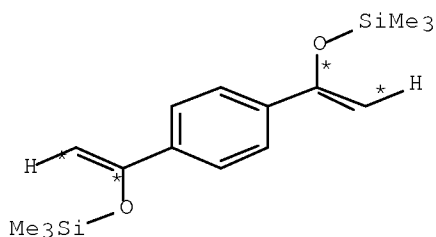
RGT H 497-19-8 Na2CO3

PRO F 1006389-40-7

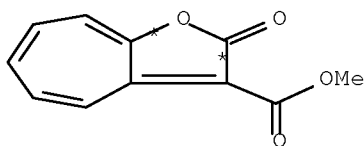
NTE stereoselective

RX(4) OF 6 COMPOSED OF RX(1), RX(2)

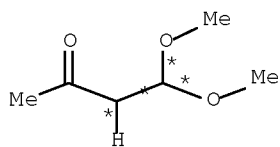
RX(4) A + 2 B + 2 E ==> F



A

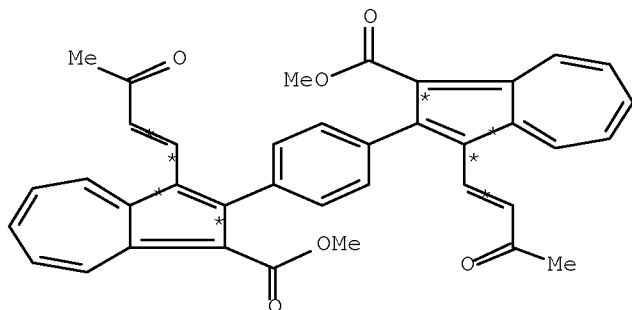


2 B



2 E

2  
STEPS  
→



F  
YIELD 28%

RX(1) RCT A 183060-22-2, B 50603-71-9  
PRO C 1006389-39-4  
SOL 91-17-8 Decalin  
CON 4 hours, reflux  
NTE modified Terasaki-Takase azulene reaction

RX(2) RCT C 1006389-39-4, E 5436-21-5

STAGE(1)  
RGT G 16872-11-0 HBF<sub>4</sub>

STAGE(2)  
RGT H 497-19-8 Na<sub>2</sub>CO<sub>3</sub>

PRO F 1006389-40-7  
NTE stereoselective

L46 ANSWER 2 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 143:153252 CASREACT [Full-text](#)

TITLE: A convenient synthesis and chemical properties of  
3-acylamino-6-polyfluoroalkyl-2H-pyran-2-ones

AUTHOR(S): Gerus, Igor I.; Tolmachova, Nataliya A.; Vdovenko,  
Sergey I.; Froehlich, Roland; Haufe, Guenter

CORPORATE SOURCE: Institute of Bioorganic Chemistry and Petrochemistry  
NASU, Kiev, 02094, Ukraine

SOURCE: Synthesis (2005), (8), 1269-1278

CODEN: SYNTBF; ISSN: 0039-7881

PUBLISHER: Georg Thieme Verlag

DOCUMENT TYPE: Journal

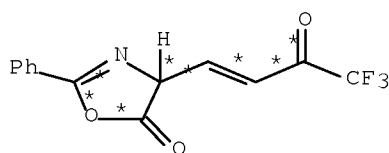
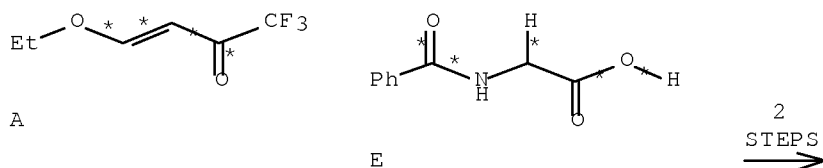
LANGUAGE: English

AB A number of 3-acylamino-6-polyfluoroalkyl-2H-pyran-2-ones were synthesized from  $\beta$ -alkoxyvinyl polyfluoroalkyl ketones and N-acylglycines in acetic anhydride in high yield. The reactions of 6-trifluoromethyl-3-benzoylamino-2H-pyran-2-one with O- and N-nucleophiles were studied and 3-N-benzoylamino-6-hydroxy-6-trifluoromethyl-5,6-dihydro-2H-pyran-2-one, 3-N-benzoylamino-6-hydroxy-6-trifluoromethyl-5,6-dihydro-2H-pyridin-2-one, and N- and O-substituted 3-(N-benzoylamino)-6-trifluoromethyl-2H-pyridin-2-ones were synthesized.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/569486

RX(30) OF 53 COMPOSED OF RX(2), RX(12)  
RX(30) A + E ==> Y



Y  
YIELD 93%

RX(2) RCT A 17129-06-5, E 495-69-2  
PRO F 312615-59-1  
SOL 108-24-7 Ac2O  
CON 6 hours, 60 deg C

RX(12) RCT F 312615-59-1

STAGE(1)

RGT Z 1310-58-3 KOH  
SOL 68-12-2 DMF  
CON 2 hours, 60 deg C

STAGE(2)

RGT AA 7647-01-0 HCl  
SOL 7732-18-5 Water  
CON pH 3

PRO Y 860454-19-9

L46 ANSWER 3 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 143:78029 CASREACT [Full-text](#)

TITLE: A practical synthesis of 3-indolyl  
 $\alpha,\beta$ -unsaturated carbonyl compounds

AUTHOR(S): Wang, Weiqi; Ikemoto, Tetsuya

CORPORATE SOURCE: Fine Chemicals Research Laboratory, Ltd., Sumitomo  
Chemical Co., Nishiyodogawa-ku, Osaka, 555-0021, Japan

SOURCE: Tetrahedron Letters (2005), 46(22), 3875-3878

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

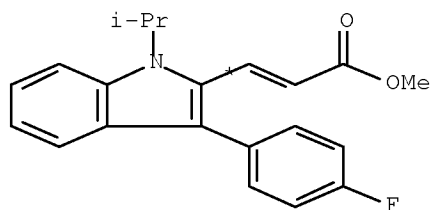
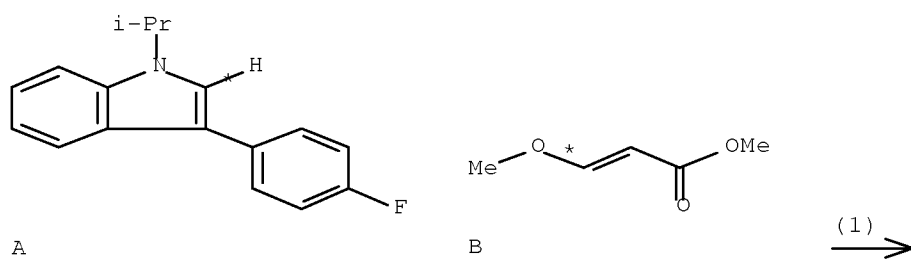
10/569486

LANGUAGE: English

AB An acid-catalyzed practical synthesis of 3-indolyl  $\alpha,\beta$ -unsatd. carbonyl compds. using Me 3-methoxyacrylate, Me 3,3-dimethoxypropionate, or 1,1-dimethoxy-3-butanone is reported. HCl aqueous solution (35%) catalyzes this reaction efficiently in acetic acid. One of the most favorable substrates is 3-(4-fluorophenyl)-1-isopropyl-1H-indole, which reacts nearly quant. to give the corresponding  $\alpha,\beta$ -unsatd. ester, and the scope of the reaction can be extended to some electron-rich benzene derivs.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 11 A + B ==&gt; C

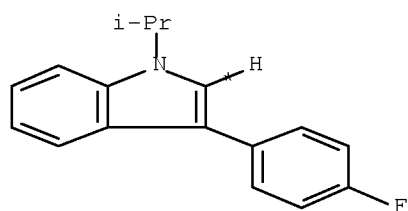


YIELD 94%

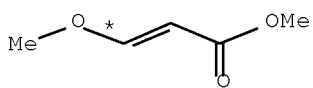
RX(1) RCT A 93957-49-4, B 5788-17-0  
 PRO C 145797-77-9  
 CAT 7647-01-0 HCl  
 SOL 7732-18-5 Water, 64-19-7 AcOH  
 CON 15 hours, 25 deg C  
 NTE optimization study, similar yield is obtained with POCl3 as a catalyst

RX(2) OF 11 A + B ==&gt; C

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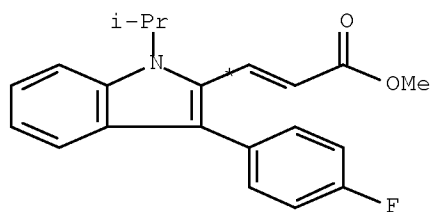


A



B

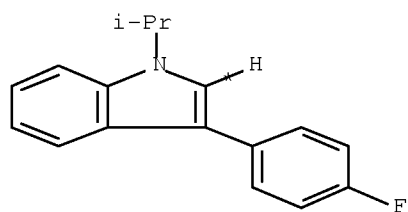
(2)  $\longrightarrow$



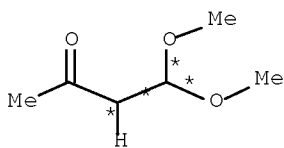
C  
YIELD 95%

RX(2)      RCT    A 93957-49-4, B 5768-17-0  
              PRO    C 145797-77-9  
              CAT    10025-87-3 POC13  
              SOL    7732-18-5 Water, 64-19-7 AcOH  
              CON    9 hours, 25 deg C  
              NTE    optimization study, optimized on catalyst and solvent

RX(3) OF 11      A + B  $\implies$  C



A

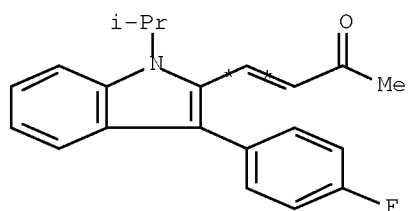


H

(3)  $\longrightarrow$



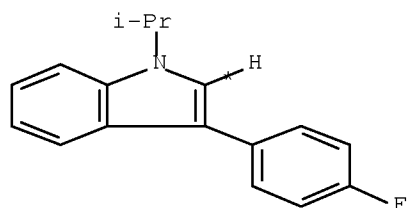
10/569486



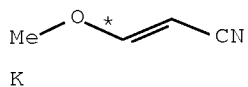
I  
YIELD 50%

RX(3)      RCT   A 93957-49-4, H 5436-21-5  
              PRO   I 847646-86-0  
              CAT   7647-01-0 HCl  
              SOL   7732-18-5 Water, 64-18-6 HCO<sub>2</sub>H  
              CON   18 hours, 25 deg C

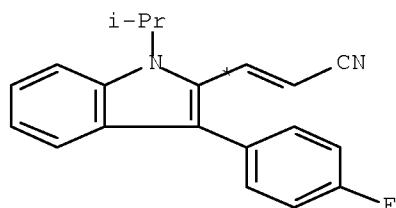
RX(4) OF 11      A + K ==> L



A



(4) →

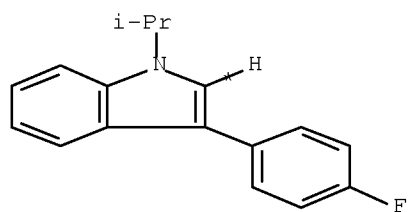


L  
YIELD 36%

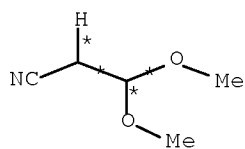
RX(4)      RCT   A 93957-49-4, K 69194-03-2  
              PRO   L 847646-85-9  
              CAT   10025-87-3 POCl<sub>3</sub>  
              SOL   7732-18-5 Water, 64-19-7 AcOH  
              CON   15 hours, 25 deg C

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RX(5) OF 11      A + M ==> L

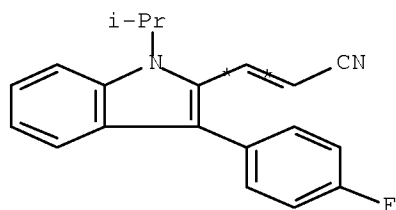


A



M

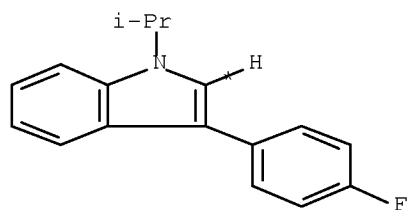
(5)  $\longrightarrow$



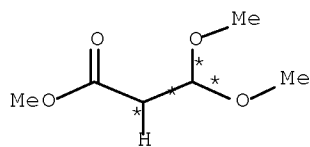
L  
YIELD 25%

RX(5)      RCT    A 93957-49-4, M 57597-62-3  
              PRO    L 847646-85-9  
              CAT    7647-01-0 HCl  
              SOL    7732-18-5 Water, 64-19-7 AcOH  
              CON    18 hours, 25 deg C

RX(6) OF 11      A + N ==> C



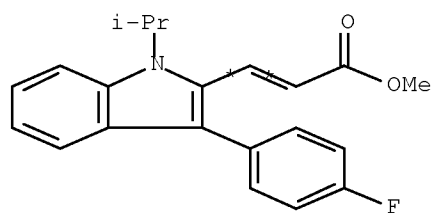
A



N

(6)  $\longrightarrow$

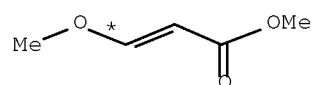
10/569486



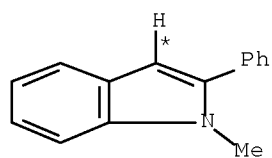
<sup>C</sup>  
YIELD 95%

RX(6)        RCT    A 93957-49-4, N 7424-91-1  
               RGT    O 108-24-7 Ac2O  
               PRO    C 145797-77-9  
               CAT    10035-10-6 HBr  
               SOL    64-19-7 AcOH  
               CON    5 hours, 25 deg C

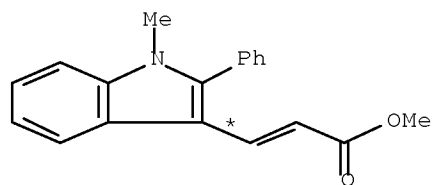
RX(7) OF 11        B    +    Q    ==>    R



B



Q

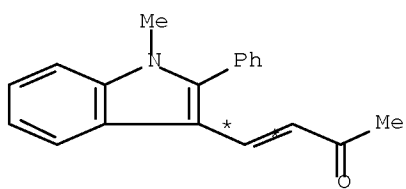
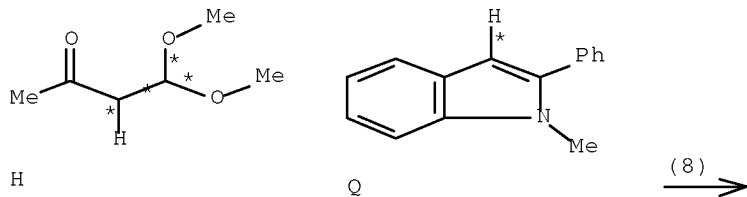


<sup>R</sup>  
YIELD 82%

RX(7)        RCT    B 5788-17-0, Q 3558-24-5  
               PRO    R 141854-06-0  
               CAT    10025-87-3 POC13  
               SOL    7732-18-5 Water, 64-19-7 AcOH  
               CON    7 hours, 25 deg C

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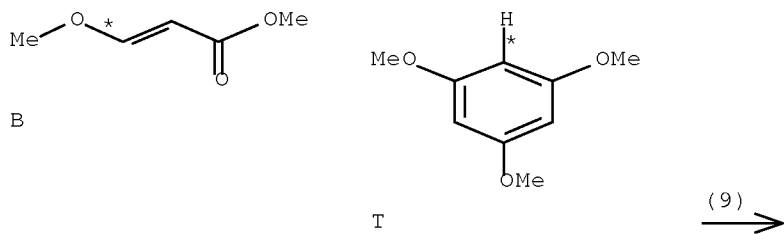
RX(8) OF 11 H + Q ==> S



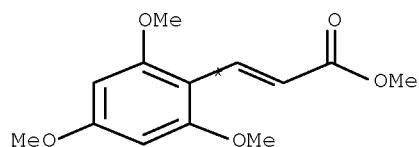
S  
YIELD 89%

RX(8) RCT H 5436-21-5, Q 3558-24-5  
PRO S 847646-87-1  
CAT 7647-01-0 HCl  
SOL 7732-18-5 Water, 64-19-7 AcOH  
CON 14 hours, 25 deg C

RX(9) OF 11 B + T ==> U



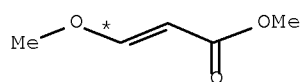
10/569486



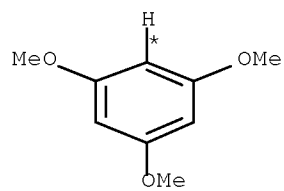
U  
YIELD 92%

RX(9)      RCT   B 5788-17-0, T 621-23-8  
              PRO   U 847646-83-7  
              CAT   10025-87-3 POC13  
              SOL   7732-18-5 Water, 64-19-7 AcOH  
              CON   5 hours, 25 deg C  
              NTE   HCl a a catalyst provided higher yield

RX(10) OF 11      B   +   T   ==>   U

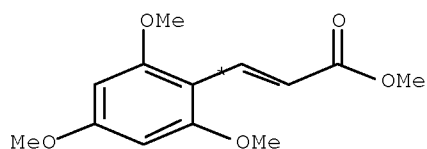


B



T

(10)  
→

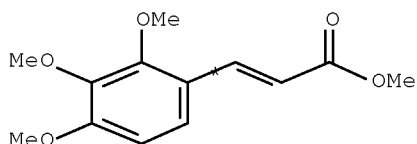
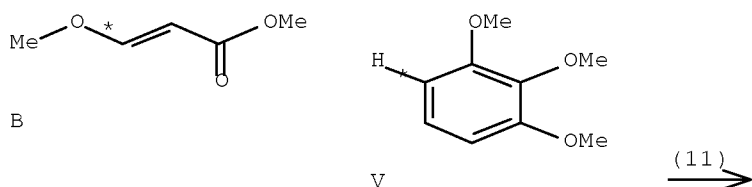


U  
YIELD 98%

RX(10)      RCT   B 5788-17-0, T 621-23-8  
              PRO   U 847646-83-7  
              CAT   7647-01-0 HCl  
              SOL   7732-18-5 Water, 64-19-7 AcOH  
              CON   1 hour, 25 deg C

RX(11) OF 11      B   +   V   ==>   W

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W  
YIELD 25%

RX(11) RCT B 5788-17-0, V 634-36-6  
PRO W 116406-21-4  
CAT 10025-87-3 POC13  
SOL 7732-18-5 Water, 64-19-7 AcOH  
CON 18 hours, 25 deg C

L46 ANSWER 4 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 140:16915 CASREACT [Full-text](#)  
TITLE: Synthesis and Biological Evaluation of 5-Substituted  
Derivatives of the Potent Antiherpes Agent  
(north)-Methanocarbathymine  
AUTHOR(S): Russ, Pamela; Schelling, Pierre; Scapozza, Leonardo;  
Folkers, Gerd; De Clercq, Erik; Marquez, Victor E.  
CORPORATE SOURCE: Laboratory of Medicinal Chemistry, Center for Cancer  
Research, National Cancer Institute at Frederick,  
Frederick, MD, 21702, USA  
SOURCE: Journal of Medicinal Chemistry (2003), 46(23),  
5045-5054  
CODEN: JMCMAR; ISSN: 0022-2623  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The conformationally locked nucleoside, (north)-methanocarbathymine, is a potent and selective anti-herpes agent effective against herpes simplex type 1 (HSV1) and type 2 (HSV2) viruses. Here we report on the synthesis and biol. evaluation of a small set of 5-substituted pyrimidine nucleosides belonging to the same class of bicyclo[3.1.0]hexane nucleosides. Both the 5-bromovinyl and the 5-bromo analog appeared to be exclusive substrates of HSV1 thymidine kinase (TK), contrasting with the 5-iodo analog, which was significantly phosphorylated by the human cytosolic TK. The binding affinity constant and catalytic turnover for HSV1 TK were measured to assess the influence of the substitution on these parameters. In the plaque reduction and cytotoxicity assays, the 5-bromo analog showed good activity against HSV1 and HSV2 with less general toxicity than (north)-methanocarbathymine. Against varicella-zoster virus (VZV), the north-locked 5-bromovinyl analog proved to be as

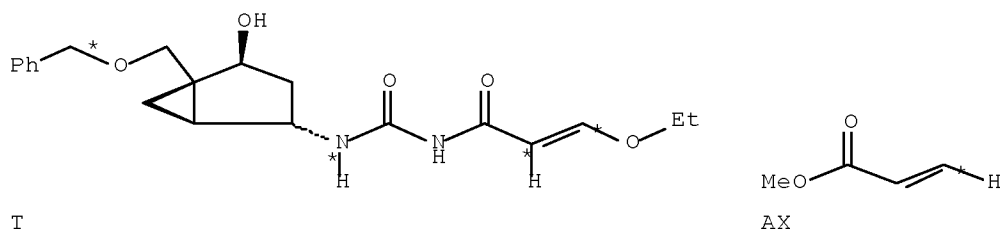
10/569486

potent as its conformationally unlocked 2'-deoxyribose equivalent BVDU. The three compds. were also tested in vitro as prodrugs used in a gene therapy context on three osteosarcoma cell lines, either deficient in TK (TK-), nontransduced, or stably transduced with HSV1 TK. The 5-iodo compound (CC50  $25 \pm 7 \mu\text{M}$ ) was more efficient than ganciclovir (GCV, CC50  $75 \pm 35 \mu\text{M}$ ) in inhibiting growth of HSV1-TK transfected cells and less inhibitory than GCV toward TK- cells, whereas the 5-bromo compound inhibited transfected and nontransfected cell lines in a relatively similar dose-dependent manner.

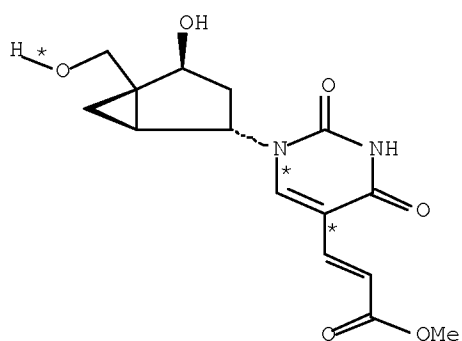
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(42) OF 63 COMPOSED OF RX(5), RX(6), RX(8), RX(15)

RX(42) T + AX ==> AE



4  
STEPS  
→



YIELD 48%

RX(5) RCT T 391679-36-0

STAGE(1)

RGT V 7664-93-9 H2SO4

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SOL 7732-18-5 Water, 64-17-5 EtOH  
CON 1 hour, reflux

STAGE(2)

RGT D 1310-73-2 NaOH  
SOL 7732-18-5 Water  
CON neutralized

PRO U 391679-37-1

RX(6) RCT U 391679-37-1  
RGT Y 7553-56-2 I2, Z 7697-37-2 HNO3  
PRO X 391679-39-3  
SOL 7732-18-5 Water, 123-91-1 Dioxane  
CON 1 hour, 100 deg C  
NTE regioselective

RX(8) RCT X 391679-39-3

STAGE(1)

RGT R 10294-34-5 BC13  
SOL 75-09-2 CH2Cl2  
CON 1 hour, -78 deg C

STAGE(2)

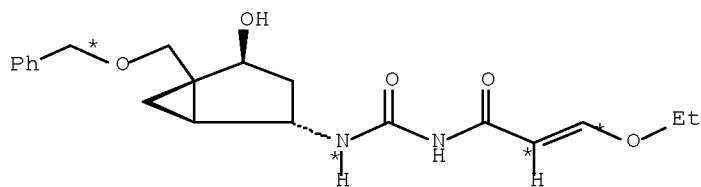
SOL 67-56-1 MeOH

PRO Q 391679-34-8

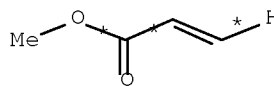
RX(15) RCT AX 96-33-3, Q 391679-34-8  
RGT AY 121-44-8 Et3N  
PRO AE 391679-42-8  
CAT 3375-31-3 Pd(OAc)2, 603-35-0 PPh3  
SOL 123-91-1 Dioxane  
CON 4 hours, 78 deg C  
NTE stereoselective

RX(58) OF 63 COMPOSED OF RX(5), RX(6), RX(8), RX(15), RX(10), RX(11)

RX(58) T + AX ==> AI



T

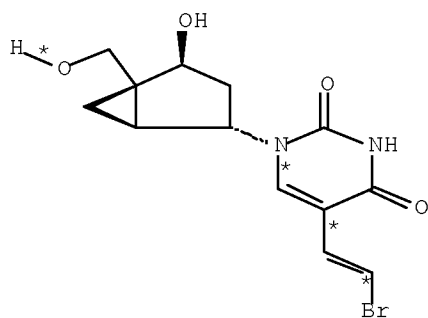


AX

6  
STEPS  
→



10/569486



AI  
YIELD 25%

RX(5) RCT T 391679-36-0

STAGE(1)  
RGT V 7664-93-9 H2SO4  
SOL 7732-18-5 Water, 64-17-5 EtOH  
CON 1 hour, reflux

STAGE(2)  
RGT D 1310-73-2 NaOH  
SOL 7732-18-5 Water  
CON neutralized

PRO U 391679-37-1

RX(6) RCT U 391679-37-1  
RGT Y 7553-56-2 I2, Z 7697-37-2 HNO3  
PRO X 391679-39-3  
SOL 7732-18-5 Water, 123-91-1 Dioxane  
CON 1 hour, 100 deg C  
NTE regioselective

RX(8) RCT X 391679-39-3

STAGE(1)  
RGT R 10294-34-5 BC13  
SOL 75-09-2 CH2Cl2  
CON 1 hour, -78 deg C

STAGE(2)  
SOL 67-56-1 MeOH

PRO Q 391679-34-8

RX(15) RCT AX 96-33-3, Q 391679-34-8  
RGT AY 121-44-8 Et3N  
PRO AE 391679-42-8  
CAT 3375-31-3 Pd(OAc)2, 603-35-0 PPh3  
SOL 123-91-1 Dioxane  
CON 4 hours, 78 deg C

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NTE stereoselective

RX(10) RCT AE 391679-42-8

STAGE(1)

RGT AG 1310-58-3 KOH

SOL 7732-18-5 Water

CON overnight, room temperature

STAGE(2)

RGT AH 7647-01-0 HCl

SOL 7732-18-5 Water

CON room temperature, pH 2

STAGE(3)

SOL 67-56-1 MeOH

PRO AF 391679-43-9

RX(11) RCT AF 391679-43-9

RGT AJ 298-14-6 KHCO<sub>3</sub>, AK 128-08-5 Bromosuccinimide

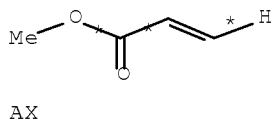
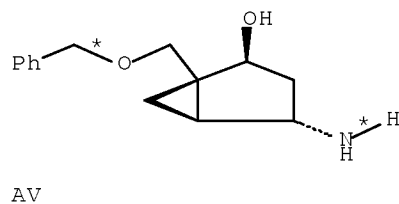
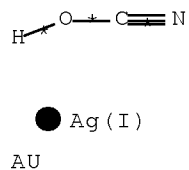
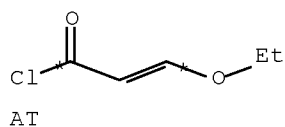
PRO AI 391679-35-9

SOL 68-12-2 DMF

CON 2.5 hours, room temperature

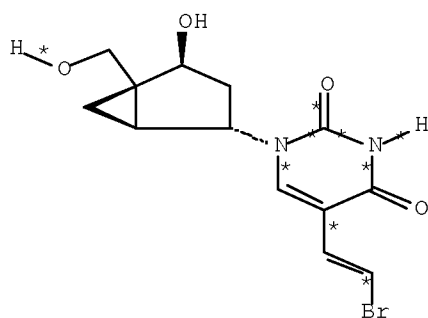
RX(59) OF 63 COMPOSED OF RX(14), RX(5), RX(6), RX(8), RX(15), RX(10), RX(11)

RX(59) AT + AU + AV + AX ==> AI



7  
 STEPS  
 →

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AI  
YIELD 25%

RX(14) RCT AT 6191-99-7, AU 3315-16-0

STAGE(1)

SOL 71-43-2 Benzene  
CON SUBSTAGE(1) 2 hours, 100 deg C  
SUBSTAGE(2) 45 minutes, reflux  
SUBSTAGE(3) reflux -> room temperature

STAGE(2)

RCT AV 191480-80-5  
SOL 68-12-2 DMF  
CON SUBSTAGE(1) 0 deg C  
SUBSTAGE(2) overnight, 0 deg C -> room temperature

PRO T 391679-36-0

RX(5) RCT T 391679-36-0

STAGE(1)

RGT V 7664-93-9 H2SO4  
SOL 7732-18-5 Water, 64-17-5 EtOH  
CON 1 hour, reflux

STAGE(2)

RGT D 1310-73-2 NaOH  
SOL 7732-18-5 Water  
CON neutralized

PRO U 391679-37-1

RX(6) RCT U 391679-37-1  
RGT Y 7553-56-2 I2, Z 7697-37-2 HNO3  
PRO X 391679-39-3  
SOL 7732-18-5 Water, 123-91-1 Dioxane  
CON 1 hour, 100 deg C  
NTE regioselective

RX(8) RCT X 391679-39-3

STAGE(1)

RGT R 10294-34-5 BC13  
SOL 75-09-2 CH2Cl2

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CON 1 hour, -78 deg C

STAGE(2)

SOL 67-56-1 MeOH

PRO Q 391679-34-8

RX(15) RCT AX 96-33-3, Q 391679-34-8  
RGT AY 121-44-8 Et3N  
PRO AE 391679-42-8  
CAT 3375-31-3 Pd(OAc)2, 603-35-0 PPh3  
SOL 123-91-1 Dioxane  
CON 4 hours, 78 deg C  
NTE stereoselective

RX(10) RCT AE 391679-42-8

STAGE(1)

RGT AG 1310-58-3 KOH

SOL 7732-18-5 Water

CON overnight, room temperature

STAGE(2)

RGT AH 7647-01-0 HCl

SOL 7732-18-5 Water

CON room temperature, pH 2

STAGE(3)

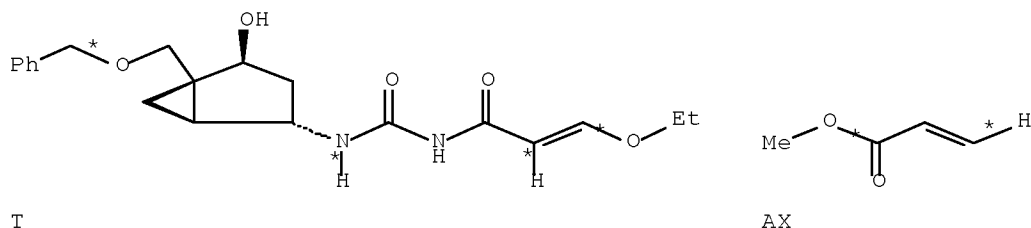
SOL 67-56-1 MeOH

PRO AF 391679-43-9

RX(11) RCT AF 391679-43-9  
RGT AJ 298-14-6 KHCO3, AK 128-08-5 Bromosuccinimide  
PRO AI 391679-35-9  
SOL 68-12-2 DMF  
CON 2.5 hours, room temperature

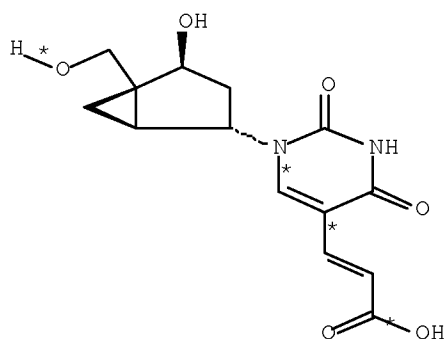
RX(60) OF 63 COMPOSED OF RX(5), RX(6), RX(8), RX(15), RX(10)

RX(60) T + AX ==> AF



5  
STEPS  
→

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AF  
YIELD 87%

RX(5) RCT T 391679-36-0

STAGE(1)  
RGT V 7664-93-9 H2SO4  
SOL 7732-18-5 Water, 64-17-5 EtOH  
CON 1 hour, reflux

STAGE(2)  
RGT D 1310-73-2 NaOH  
SOL 7732-18-5 Water  
CON neutralized

PRO U 391679-37-1

RX(6) RCT U 391679-37-1  
RGT Y 7553-56-2 I2, Z 7697-37-2 HNO3  
PRO X 391679-39-3  
SOL 7732-18-5 Water, 123-91-1 Dioxane  
CON 1 hour, 100 deg C  
NTE regioselective

RX(8) RCT X 391679-39-3

STAGE(1)  
RGT R 10294-34-5 BC13  
SOL 75-09-2 CH2Cl2  
CON 1 hour, -78 deg C

STAGE(2)  
SOL 67-56-1 MeOH

PRO Q 391679-34-8

RX(15) RCT AX 96-33-3, Q 391679-34-8  
RGT AY 121-44-8 Et3N  
PRO AE 391679-42-8  
CAT 3375-31-3 Pd(OAc)2, 603-35-0 PPh3

10/569486

SOL 123-91-1 Dioxane  
CON 4 hours, 78 deg C  
NTE stereoselective

RX(10) RCT AE 391679-42-8

STAGE(1)

RGT AG 1310-58-3 KOH  
SOL 7732-18-5 Water  
CON overnight, room temperature

STAGE(2)

RGT AH 7647-01-0 HCl  
SOL 7732-18-5 Water  
CON room temperature, pH 2

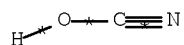
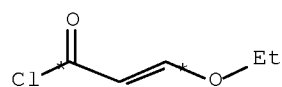
STAGE(3)

SOL 67-56-1 MeOH

PRO AF 391679-43-9

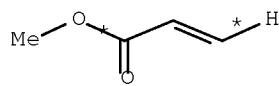
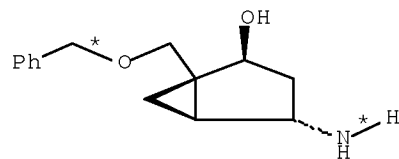
RX(61) OF 63 COMPOSED OF RX(14), RX(5), RX(6), RX(8), RX(15), RX(10)

RX(61) AT + AU + AV + AX ==> AF



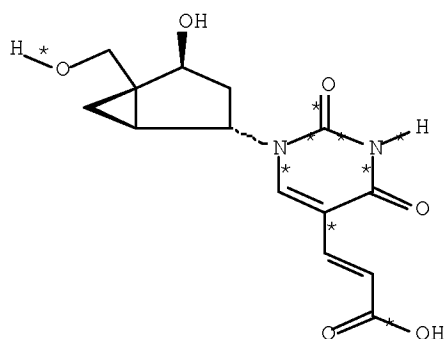
● Ag(I)

AU



6  
STEPS  
→

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AF  
YIELD 87%

RX(14) RCT AT 6191-99-7, AU 3315-16-0

STAGE(1)

SOL 71-43-2 Benzene

CON SUBSTAGE(1) 2 hours, 100 deg C

SUBSTAGE(2) 45 minutes, reflux

SUBSTAGE(3) reflux -> room temperature

STAGE(2)

RCT AV 191480-80-5

SOL 68-12-2 DMF

CON SUBSTAGE(1) 0 deg C

SUBSTAGE(2) overnight, 0 deg C -> room temperature

PRO T 391679-36-0

RX(5) RCT T 391679-36-0

STAGE(1)

RGT V 7664-93-9 H2SO4

SOL 7732-18-5 Water, 64-17-5 EtOH

CON 1 hour, reflux

STAGE(2)

RGT D 1310-73-2 NaOH

SOL 7732-18-5 Water

CON neutralized

PRO U 391679-37-1

RX(6) RCT U 391679-37-1

RGT Y 7553-56-2 I2, Z 7697-37-2 HNO3

PRO X 391679-39-3

SOL 7732-18-5 Water, 123-91-1 Dioxane

CON 1 hour, 100 deg C

NTE regioselective

RX(8) RCT X 391679-39-3

STAGE(1)

RGT R 10294-34-5 BC13

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SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>  
CON 1 hour, -78 deg C

STAGE(2)  
SOL 67-56-1 MeOH

PRO Q 391679-34-8

RX(15) RCT AX 96-33-3, Q 391679-34-8  
RGT AY 121-44-8 Et<sub>3</sub>N  
PRO AE 391679-42-8  
CAT 3375-31-3 Pd(OAc)<sub>2</sub>, 603-35-0 PPh<sub>3</sub>  
SOL 123-91-1 Dioxane  
CON 4 hours, 78 deg C  
NTE stereoselective

RX(10) RCT AE 391679-42-8

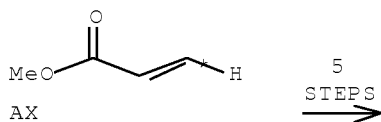
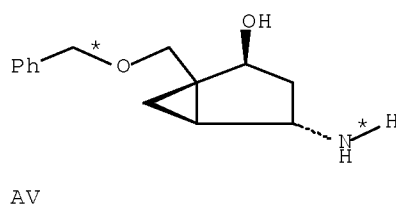
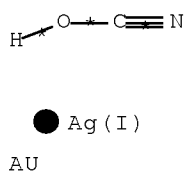
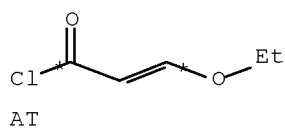
STAGE(1)  
RGT AG 1310-58-3 KOH  
SOL 7732-18-5 Water  
CON overnight, room temperature

STAGE(2)  
RGT AH 7647-01-0 HCl  
SOL 7732-18-5 Water  
CON room temperature, pH 2

STAGE(3)  
SOL 67-56-1 MeOH

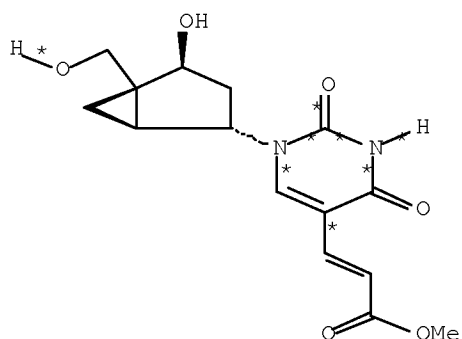
PRO AF 391679-43-9

RX(62) OF 63 COMPOSED OF RX(14), RX(5), RX(6), RX(8), RX(15)  
RX(62) AT + AU + AV + AX ==> AE





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AE  
YIELD 48%

RX(14) RCT AT 6191-99-7, AU 3315-16-0

STAGE(1)

SOL 71-43-2 Benzene

CON SUBSTAGE(1) 2 hours, 100 deg C

SUBSTAGE(2) 45 minutes, reflux

SUBSTAGE(3) reflux -> room temperature

STAGE(2)

RCT AV 191480-80-5

SOL 68-12-2 DMF

CON SUBSTAGE(1) 0 deg C

SUBSTAGE(2) overnight, 0 deg C -> room temperature

PRO T 391679-36-0

RX(5) RCT T 391679-36-0

STAGE(1)

RGT V 7664-93-9 H2SO4

SOL 7732-18-5 Water, 64-17-5 EtOH

CON 1 hour, reflux

STAGE(2)

RGT D 1310-73-2 NaOH

SOL 7732-18-5 Water

CON neutralized

PRO U 391679-37-1

RX(6) RCT U 391679-37-1

RGT Y 7553-56-2 I2, Z 7697-37-2 HNO3

PRO X 391679-39-3

SOL 7732-18-5 Water, 123-91-1 Dioxane

CON 1 hour, 100 deg C

NTE regioselective

RX(8) RCT X 391679-39-3

STAGE(1)

RGT R 10294-34-5 BC13

10/569486

SOL 75-09-2 CH2Cl2  
CON 1 hour, -78 deg C

STAGE(2)  
SOL 67-56-1 MeOH

PRO Q 391679-34-8

RX(15) RCT AX 96-33-3, Q 391679-34-8  
RGT AY 121-44-8 Et3N  
PRO AE 391679-42-8  
CAT 3375-31-3 Pd(OAc)2, 603-35-0 PPh3  
SOL 123-91-1 Dioxane  
CON 4 hours, 78 deg C  
NTE stereoselective

L46 ANSWER 5 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 138:271677 CASREACT Full-text

TITLE: Process for the preparation of 1,5-diarylpurazoles  
useful as COX-2 inhibitors, including celecoxib, via  
cyclocondensation of arylalkynones with arylhydrazines

INVENTOR(S): Reddy, M. V. Ramana; Bell, Stanley C.

PATENT ASSIGNEE(S): Onconova Therapeutics, Inc., USA

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

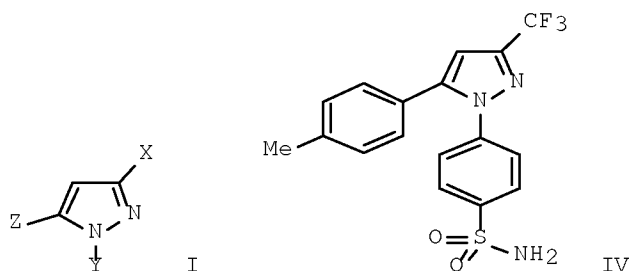
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024958	A2	20030327	WO 2002-US29581	20020918
WO 2003024958	A3	20031211		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002336593	A1	20030401	AU 2002-336593	20020918
US 20030109709	A1	20030612	US 2002-246565	20020918
US 6906196	B2	20050614		
EP 1436285	A2	20040714	EP 2002-773451	20020918
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
JP 2005508320	T	20050331	JP 2003-528805	20020918
NZ 532346	A	20051028	NZ 2002-532346	20020918
IN 2004KN00496	A	20060818	IN 2004-KN496	20040415
US 20050209459	A1	20050922	US 2005-118261	20050429
PRIORITY APPLN. INFO.:			US 2001-323479P	20010918
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			WO 2002-US29581	20020918

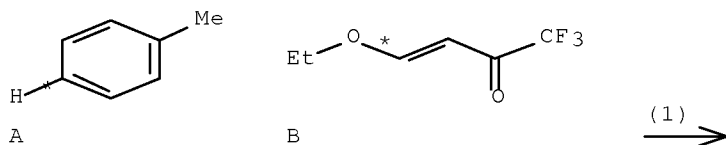
OTHER SOURCE(S): MARPAT 138:271677

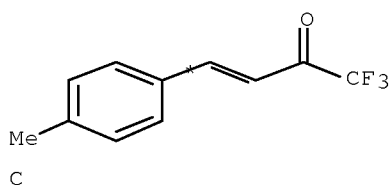
GI



AB Provided are processes for the preparation of diarylpyrazole derivs. I [wherein: X = trihalomethyl, C1-C6 alkyl, C6H3R1R2; R1, R2 = H, halo, OH, NO2, C1-C6 alkyl, C1-C6 alkoxy, CO2H, C1-C6 trihaloalkyl, cyano, alkylsulfonyl, sulfamyl, phosphonato, or hydroxyalkyl; Y, Z = (un)substituted (hetero)aryl]. Also provided are synthetic intermediates that are useful in the preparation of I. The processes involve cyclocondensation of arylalkynones ZC.tplbond.CCOX with arylhydrazines YNHNH2 or salts thereof. The claimed compds. include the above arylalkynones, and also a subset of I, the latter with X = CF3, Y = 4-H2NSO2C6H4, Z = (un)substituted 3-indolyl. Compds. I are well-known inhibitors of cyclooxygenase-2 (COX-2), and are useful for treatment of inflammation and related disorders, including arthritis (no data). The invention process uses readily available and inexpensive starting materials, and provides high yields of I with simplified isolation and purification steps. For example, alkenylation of toluene by EtOCH:CHCOCF3 and ZnCl2 in CH2Cl2 gives 4-MeC6H4CH:CHCOCF3, which is brominated (Br2 in CHCl3 at room temperature) and dehydrobrominated (KOH in refluxing EtOH) to give 4-MeC6H4C.tplbond.CCOCF3 (II). In a sep. reaction, sulfanilamide is diazotized (NaNO2, HCl) and reduced (SnCl2, HCl) to give 4-H2NSO2C6H4NHNH2 as the hydrochloride (III). Cyclization of II with III in refluxing EtOH over 4 h gives I [X = CF3, Y = 4-H2NSO2C6H4, Z = 4-MeC6H4], i.e., the drug celecoxib (IV). Similarly prepared was I [X = CH3, Y = 4-H2NSO2C6H4, Z = Ph].

RX(1) OF 15      A + E ==> C...





RX(1) RCT A 108-88-3, B 17129-06-5  
 PRO C 232947-12-5  
 CAT 7646-85-7 ZnCl2  
 SOL 75-09-2 CH2Cl2  
 CON 3 hours, 22 deg C  
 NTE scalable

L46 ANSWER 6 OF 24 CASREACT COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 138:271673 CASREACT Full-text  
 TITLE: Process for the preparation of 1,5-diarylpyrazoles  
 useful as COX-2 inhibitors, including celecoxib, via  
 cyclocondensation of phenylalkynones with  
 phenylhydrazines  
 INVENTOR(S): Reddy, M. V. Ramana; Bell, Stanley C.  
 PATENT ASSIGNEE(S): Onconova Therapeutics, Inc., USA  
 SOURCE: PCT Int. Appl., 14 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

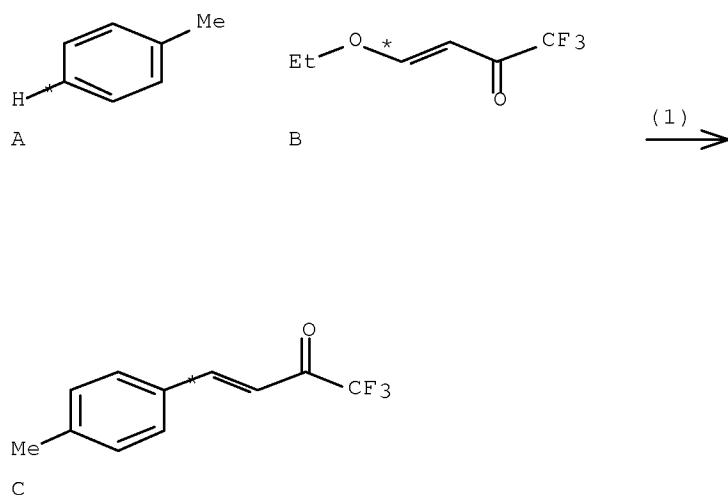
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024400	A2	20030327	WO 2002-US29566	20020918
WO 2003024400	A3	20030626		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002330042	A1	20030401	AU 2002-330042	20020918
US 20030096853	A1	20030522	US 2002-245949	20020918
US 6579988	B2	20030617		
US 20030199707	A1	20031023	US 2003-423790	20030425
US 6706927	B2	20040316		
PRIORITY APPLN. INFO.:			US 2001-323006P	20010918
			US 2002-245949	20020918
			WO 2002-US29566	20020918

OTHER SOURCE(S): MARPAT 138:271673  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Provided are processes for the preparation of diarylpyrazole derivs. I [wherein R1, R3 and R4 are independently selected from H, halogen, OH, NO2, lower alkyl, lower alkoxy, CO2H, C1-C6 trihaloalkyl, and cyano; and R2 is amino or lower alkyl]. Also provided are synthetic intermediates that are useful in the preparation of I. The processes involves cyclocondensation of phenylalkynones II with phenylhydrazines III or salts thereof. The claimed intermediates are the phenylalkynones II. Compds. I are well-known inhibitors of cyclooxygenase-2 (COX-2), and are useful for treatment of inflammation and related disorders, including arthritis (no data). The invention process uses readily available and inexpensive starting materials, and provides high yields of I with simplified isolation and purification steps. For example, alkenylation of toluene by EtOCH:CHCOCF3 and ZnCl2 in CH2Cl2 gives 4-MeC6H4CH:CHCOCF3, which is brominated (Br2 in CHCl3 at room temperature) and dehydrobrominated (KOH in refluxing EtOH) to give 4-MeC6H4C.tplbond.CCOCF3 (IV). In a sep. reaction, sulfanilamide is diazotized (NaNO2, HCl) and reduced (SnCl2, HCl) to give 4-H2NSO2C6H4NHNH2 as the hydrochloride (V). Cyclization of IV with V in refluxing EtOH over 4 h gives I [R1 = 4-Me, R2 = NH2, R3 = R4 = H], i.e., the drug celecoxib.

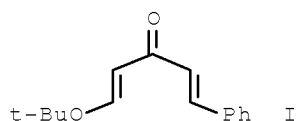
RX(1) OF 13      A + B ==> C...



RX(1)      RCT    A 108-88-3, B 17129-06-5  
              PRO    C 232947-12-5  
              CAT    7646-85-7 ZnCl2  
              SOL    75-09-2 CH2Cl2  
              CON    3 hours, 22 deg C  
              NTE    scalable

10/569486

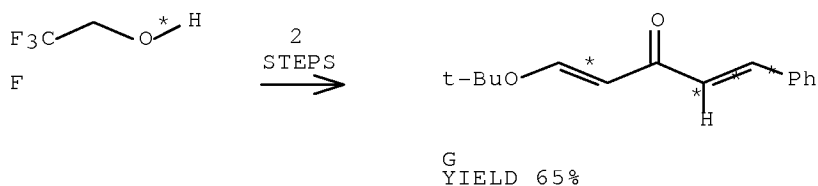
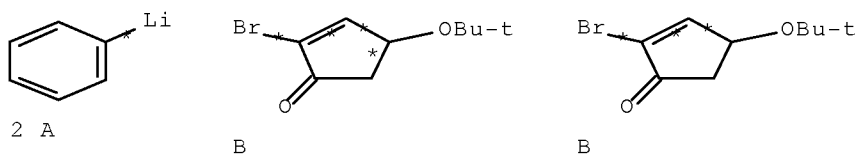
ACCESSION NUMBER: 138:89482 CASREACT [Full-text](#)  
 TITLE: The Retro-Nazarov Reaction  
 AUTHOR(S): Harmata, Michael; Lee, Dong Reyoul  
 CORPORATE SOURCE: Department of Chemistry, University of  
 Missouri-Columbia, Columbia, MO, 65211, USA  
 SOURCE: Journal of the American Chemical Society (2002),  
 124(48), 14328-14329  
 CODEN: JACSAT; ISSN: 0002-7863  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



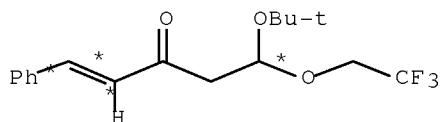
AB Treatment of 2-bromo-4-t-butoxy-2-cyclopentenone with an amine base in refluxing trifluoroethanol afforded a ring-opened product in moderate yield. The mechanism of the reaction has been formulated as a retro-Nazarov reaction in which an oxyallylic cation undergoes ring-opening to a dienone. Several other examples of the reaction have been established through a protocol involving the conjugate addition of an organocuprate to 2-bromo-4-t-butoxy-2-cyclopentenone followed by treatment of the adducts with base in refluxing trifluoroethanol to provide divinyl ketones, e.g., I.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(22) OF 31 COMPOSED OF RX(1), RX(2)  
 RX(22) 2 A + 2 B + F ==> G + H



10/569486



<sup>H</sup>  
YIELD 9%

RX(1) RCT A 591-51-5

STAGE(1)

RGT D 7681-65-4 CuI

SOL 60-29-7 Et<sub>2</sub>O

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) 15 minutes, -78 deg C

SUBSTAGE(3) 15 minutes, 0 deg C

SUBSTAGE(4) 15 minutes, room temperature

STAGE(2)

RCT B 485401-53-4

SOL 60-29-7 Et<sub>2</sub>O

CON SUBSTAGE(1) 10 minutes, -78 deg C

SUBSTAGE(2) 15 minutes, -78 deg C

SUBSTAGE(3) 10 minutes, 0 deg C

SUBSTAGE(4) 10 minutes, room temperature

PRO C 485401-54-5

RX(2) RCT C 485401-54-5, F 75-89-8

RGT I 121-44-8 Et<sub>3</sub>N

PRO G 485401-55-6, H 485401-66-9

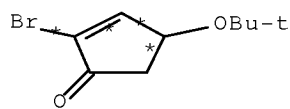
SOL 75-89-8 F<sub>3</sub>CCH<sub>2</sub>OH

CON 1 hour, reflux

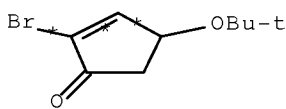
NTE optimization study, retro-Nazarov reaction, stereoselective

RX(23) OF 31 COMPOSED OF RX(3), RX(13)

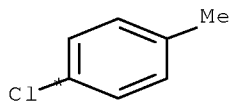
RX(23) 2 B + 2 J + F ==> AH + AI



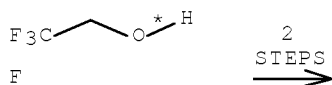
B



B



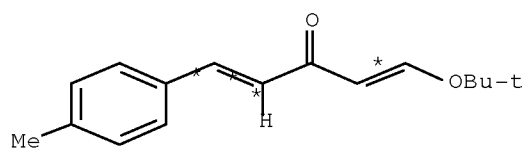
2 J



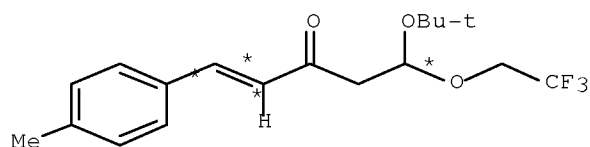
F

2  
STEPS  
→

10/569486



AH  
YIELD 52%



AI  
YIELD 9%

RX(3) RCT B 485401-53-4

STAGE(1)

RGT D 7681-65-4 CuI

SOL 60-29-7 Et2O

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) 15 minutes, -78 deg C

SUBSTAGE(3) 15 minutes, 0 deg C

SUBSTAGE(4) 15 minutes, room temperature

STAGE(2)

RCT J 106-43-4

SOL 60-29-7 Et2O

CON SUBSTAGE(1) 10 minutes, -78 deg C

SUBSTAGE(2) 15 minutes, -78 deg C

SUBSTAGE(3) 10 minutes, 0 deg C

SUBSTAGE(4) 10 minutes, room temperature

PRO K 485401-56-7

RX(13) RCT K 485401-56-7, F 75-89-8

RGT I 121-44-8 Et3N

PRO AH 485401-67-0, AI 485401-68-1

SOL 75-89-8 F3CCH2OH

CON 1 hour, reflux

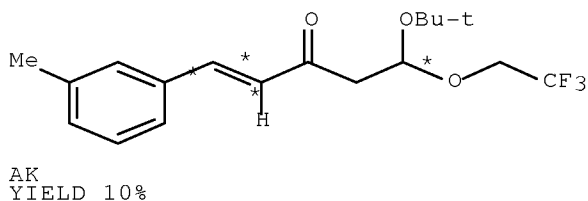
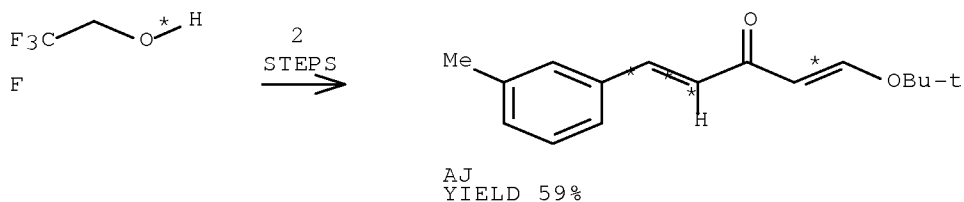
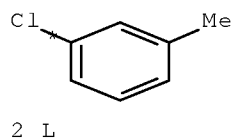
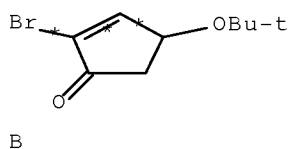
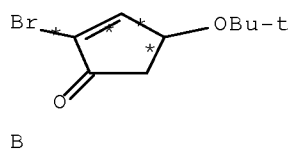
NTE retro-Nazarov reaction, stereoselective

RX(24) OF 31 COMPOSED OF RX(4), RX(14)

RX(24) 2 E + 2 L + F ==> AJ + AK



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RX(4) RCT B 485401-53-4

STAGE(1)

RGT D 7681-65-4 CuI

SOL 60-29-7 Et2O

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) 15 minutes, -78 deg C

SUBSTAGE(3) 15 minutes, 0 deg C

SUBSTAGE(4) 15 minutes, room temperature

STAGE(2)

RCT L 108-41-8

SOL 60-29-7 Et2O

CON SUBSTAGE(1) 10 minutes, -78 deg C

SUBSTAGE(2) 15 minutes, -78 deg C

SUBSTAGE(3) 10 minutes, 0 deg C

SUBSTAGE(4) 10 minutes, room temperature

PRO M 485401-57-8

RX(14) RCT M 485401-57-8, F 75-89-8

RGT I 121-44-8 Et3N

PRO AJ 485401-69-2, AK 485401-77-2

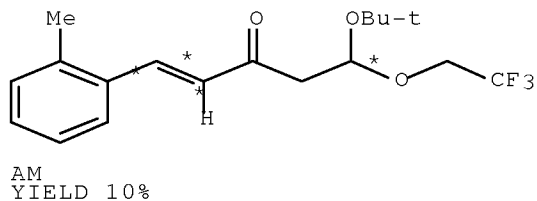
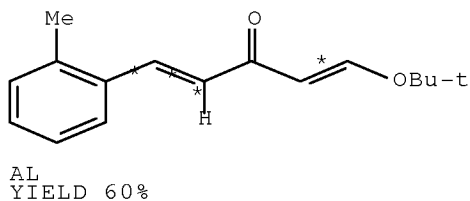
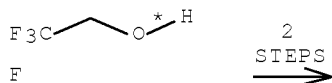
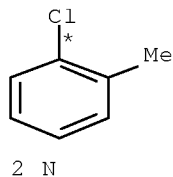
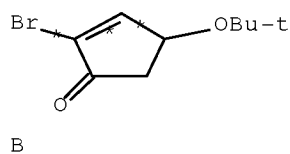
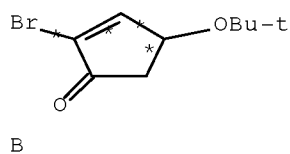
SOL 75-89-8 F3CCH2OH

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CON 1 hour, reflux  
 NTE retro-Nazarov reaction, stereoselective

RX(25) OF 31 COMPOSED OF RX(5), RX(15)

RX(25) 2 B + 2 N + F ==> AL + AM



RX(5) RCT B 485401-53-4

STAGE(1)

RGT D 7681-65-4 CuI

SOL 60-29-7 Et2O

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) 15 minutes, -78 deg C

SUBSTAGE(3) 15 minutes, 0 deg C

SUBSTAGE(4) 15 minutes, room temperature

STAGE(2)

RCT N 95-49-8

SOL 60-29-7 Et2O

CON SUBSTAGE(1) 10 minutes, -78 deg C

SUBSTAGE(2) 15 minutes, -78 deg C

SUBSTAGE(3) 10 minutes, 0 deg C

SUBSTAGE(4) 10 minutes, room temperature

PRO O 485401-58-9

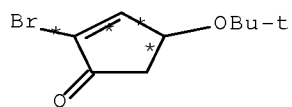
RX(15) RCT O 485401-58-9, F 75-89-8

10/569486

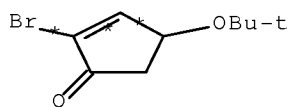
RGT I 121-44-8 Et3N  
 PRO AL 485401-70-5, AM 485401-78-3  
 SOL 75-89-8 F3CCH2OH  
 CON 1 hour, reflux  
 NTE retro-Nazarov reaction, stereoselective

RX(26) OF 31 COMPOSED OF RX(6), RX(16)

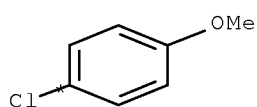
RX(26) 2 B + 2 P + F ==> AN + AO



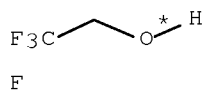
B



B

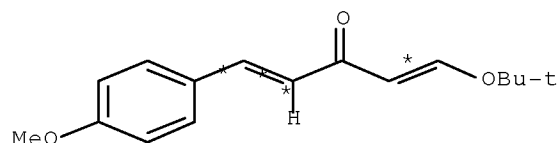


2 P

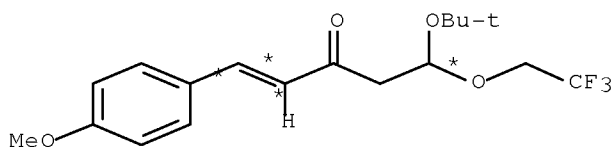


F

2  
STEPS  
→



AN  
YIELD 59%



AO  
YIELD 8%

RX(6) RCT B 485401-53-4

STAGE(1)

RGT D 7681-65-4 CuI

SOL 60-29-7 Et2O

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) 15 minutes, -78 deg C

SUBSTAGE(3) 15 minutes, 0 deg C

SUBSTAGE(4) 15 minutes, room temperature

STAGE(2)

RCT P 623-12-1

SOL 60-29-7 Et2O

CON SUBSTAGE(1) 10 minutes, -78 deg C

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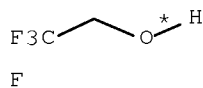
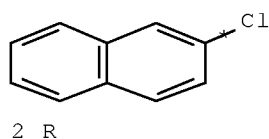
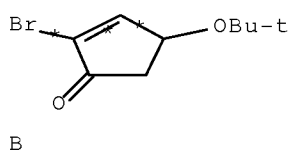
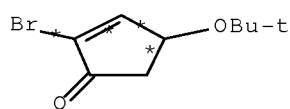
SUBSTAGE(2) 15 minutes, -78 deg C  
SUBSTAGE(3) 10 minutes, 0 deg C  
SUBSTAGE(4) 10 minutes, room temperature

PRO Q 485401-59-0

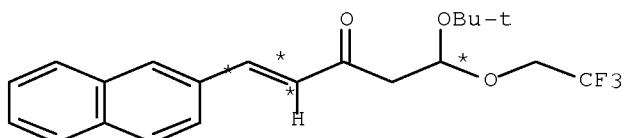
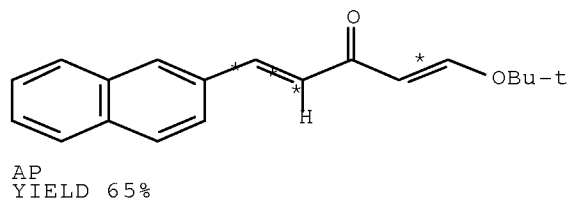
RX(16) RCT Q 485401-59-0, F 75-89-8  
RGT I 121-44-8 Et3N  
PRO AN 485401-71-6, AO 485401-79-4  
SOL 75-89-8 F3CCH2OH  
CON 1 hour, reflux  
NTE retro-Nazarov reaction, stereoselective

RX(27) OF 31 COMPOSED OF RX(7), RX(17)

RX(27) 2 B + 2 R + F ==> AP + AQ



2  
STEPS  
→



RX(7) RCT B 485401-53-4

STAGE(1)

RGT D 7681-65-4 CuI  
SOL 60-29-7 Et2O  
CON SUBSTAGE(1) room temperature -> -78 deg C  
SUBSTAGE(2) 15 minutes, -78 deg C

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SUBSTAGE(3) 15 minutes, 0 deg C  
SUBSTAGE(4) 15 minutes, room temperature

STAGE (2)

RCT R 91-58-7

SOL 60-29-7 Et20

CON SUBSTAGE(1) 10 minutes, -78 deg C

SUBSTAGE(2) 15 minutes, -78 deg C

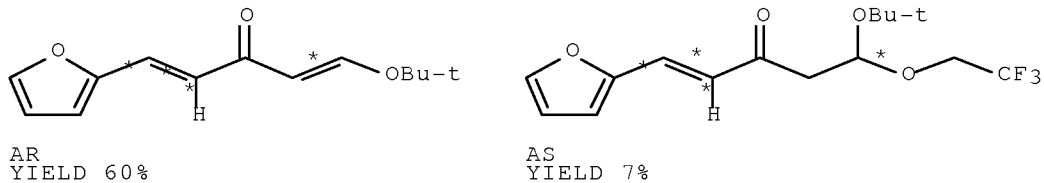
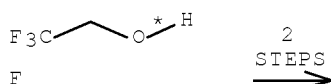
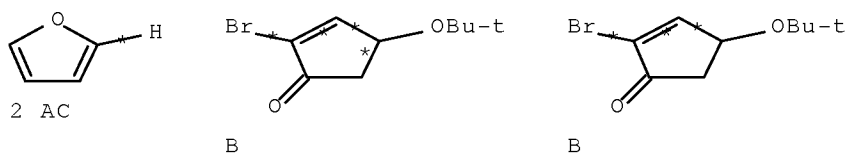
SUBSTAGE (3) 10 minutes, 0 deg C

SUBSTAGE(4) 10 minutes, room temperature

PRO S 485401-60-3

RX(17) RCT S 485401-60-3, F 75-89-8  
RGT I 121-44-8 Et3N  
PRO AP 485401-72-7, AQ 485401-80-7  
SOL 75-89-8 F3CCH2OH  
CON 1 hour, reflux  
NTE retro-Nazarov reaction, stereoselective

RX(31) OF 31 COMPOSED OF RX(11), RX(18)

$$\text{RX(31)} \quad 2 \text{ AC} + 2 \text{ B} + \text{F} \implies \text{AR} + \text{AS}$$


RX(11) RCT AC 110-00-9

STAGE (1)

RGT AE 109-72-8 BuLi

SOL 109-99-9 THF

CON SUBSTAGE (1) -78 deg C

SUBSTAGE(2) 24 hours, room temperature

STAGE(2)

RGT D 7681-65-4 CuI

SOL 60-29-7 Et2O

CON SUBSTAGE(1) 10 minutes, -78 deg C

SUBSTAGE(2) 15 hours, 0 deg C

SUBSTAGE(3) 15 hours, room temperature

STAGE(3)

RCT B 485401-53-4

CON SUBSTAGE(1) 15 minutes, -78 deg C

SUBSTAGE(2) 10 minutes, 0 deg C

SUBSTAGE(3) 15 hours, room temperature

PRO AD 485401-64-7

RX(18) RCT AD 485401-64-7, F 75-89-8  
 RGT I 121-44-8 Et3N  
 PRO AR 485401-73-8, AS 485401-81-8  
 SOL 75-89-8 F3CCH2OH  
 CON 1 hour, reflux  
 NTE retro-Nazarov reaction, stereoselective

L46 ANSWER 8 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 136:87214 CASREACT Full-text

TITLE: A 3-hydroxychromone with dramatically improved  
 fluorescence properties

AUTHOR(S): Klymchenko, Andrey S.; Ozturk, Turan; Pivovarenko,  
 Vasyl G.; Demchenko, Alexander P.

CORPORATE SOURCE: TUBITAK Marmara Research Center, Gebze-Kocaeli, 41470,  
 Turk.

SOURCE: Tetrahedron Letters (2001), 42(45), 7967-7970

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

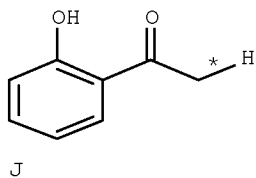
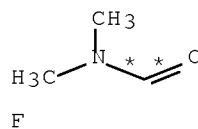
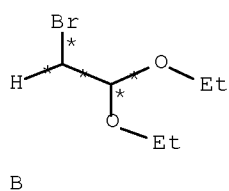
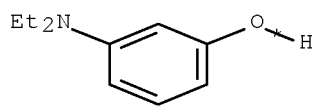
AB A new 3-hydroxychromone derivative, 2-[6-(diethylamino)benzo[b]furan-2-yl]-3-hydroxychromone, has been synthesized by a concise route. Possessing dual emission common for 3-hydroxyflavones, it exhibits strong red shifts of both absorption and fluorescence spectra, which makes it the longest wavelength fluorescent dye among all known chromones. It also demonstrates a significant increase in fluorescence quantum yield in aprotic solvents and shift in solvent-polarity-dependent switch between normal and tautomer emissive forms. This derivative offers new possibilities in designing novel mol. sensors.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

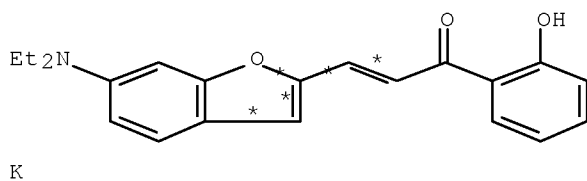
RX(8) OF 10 COMPOSED OF RX(1), RX(2), RX(3)

RX(8) A + B + F + J ==> K

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3  
STEPS  
→



```

RX(1)      RCT  A 91-68-9

            STAGE(1)
            RGT  D 7646-69-7 NaH
            SOL  68-12-2 DMF

            STAGE(2)
            RCT  B 2032-35-1
            CAT  7681-11-0 KI
            SOL  67-68-5 DMSO

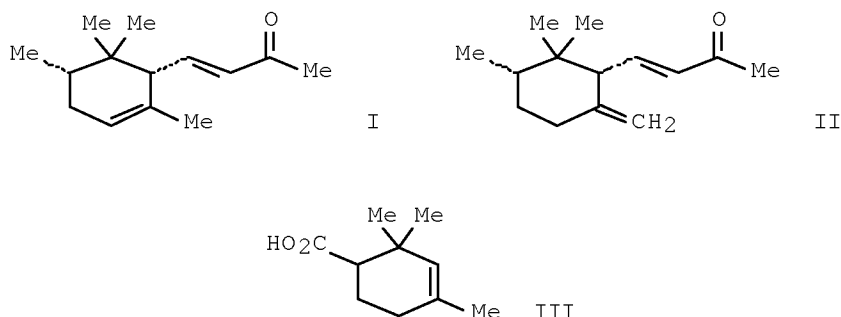
            PRO  C 108639-47-0

RX(2)      RCT  C 108639-47-0, F 68-12-2
            RGT  I 10025-87-3 POC13
            PRO  H 126174-13-8
            SOL  68-12-2 DMF

RX(3)      RCT  H 126174-13-8, J 118-93-4
            RGT  L 1310-58-3 KOH
            PRO  K 386736-83-0
            SOL  64-17-5 EtOH, 7732-18-5 Water
  
```

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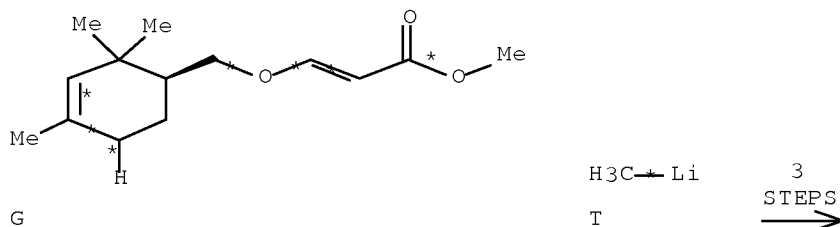
ACCESSION NUMBER: 134:178683 CASREACT Full-text  
 TITLE: Synthesis of both enantiomers of cis- $\alpha$ -irone and cis- $\gamma$ -irone, principal constituents of iris oil, via resolution of ( $\pm$ )-2,2,4-trimethyl-3-cyclohexene-1-carboxylic acid  
 AUTHOR(S): Inoue, T.; Kiyota, H.; Oritani, T.  
 CORPORATE SOURCE: Department of Applied Bioorganic Chemistry, Division of Life Science, Graduate School of Agricultural Science, Tohoku University, Sendai, Aoba-ku, 981-8555, Japan  
 SOURCE: Tetrahedron: Asymmetry (2000), 11(18), 3807-3818  
 CODEN: TASYE3; ISSN: 0957-4166  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



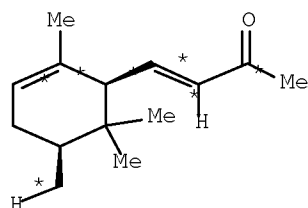
AB The principal constituents of iris oil, (-)-cis- $\alpha$ -irone (I) and (-)-cis- $\gamma$ -irone (II), and their enantiomers, were synthesized from (-)- and (+)-2,2,4-trimethyl-3-cyclohexene-1-carboxylic acids (III). The racemic acid was resolved by recrystn. of its salt with a chiral amine, or by enzymic hydrolysis of the corresponding alc. The fragrances of (-)-(1R,5S)-cis- $\alpha$ -irone and (-)-(1R,5S)-cis- $\gamma$ -irone were superior to those of (+)-(1S,5R)-cis- $\alpha$ -irone and (+)-(1S,5R)-cis- $\gamma$ -irone.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(29) OF 56 COMPOSED OF RX(4), RX(5), RX(7)  
 RX(29) G + T ==> U







U  
YIELD 68%

RX(4) RCT G 326907-23-7  
RGT K 75-75-2 MeSO<sub>3</sub>H  
PRO J 326907-24-8  
SOL 60-29-7 Et<sub>2</sub>O  
NTE stereoselective

RX(5) RCT J 326907-24-8  
RGT M 1310-73-2 NaOH  
PRO L 326907-25-9  
SOL 67-56-1 MeOH  
NTE stereoselective

RX(7) RCT L 326907-25-9

STAGE(1)

RGT V 4111-54-0 LiN(Pr-i)<sub>2</sub>  
SOL 109-99-9 THF

STAGE(2)

RGT W 124-63-0 MeSO<sub>2</sub>Cl, X 110-86-1 Pyridine  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

STAGE(3)

RGT Q 7440-66-6 Zn, Y 7681-82-5 NaI  
SOL 110-71-4 (CH<sub>2</sub>OMe)<sub>2</sub>

STAGE(4)

RCT T 917-54-4  
SOL 60-29-7 Et<sub>2</sub>O

PRO U 89888-03-9  
NTE stereoselective

L46 ANSWER 10 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 132:93182 CASREACT [Full-text](#)

TITLE: Synthesis of indolyl- and pyrrolyl-substituted  
trifluoromethyl-containing enones

AUTHOR(S): Sanin, A. V.; Nenaidenko, V. G.; Balenkova, E. S.

CORPORATE SOURCE: Faculty of Chemistry, Moscow State University, Moscow,  
119899, Russia

10/569486

SOURCE:

Russian Journal of Organic Chemistry (Translation of Zhurnal Organicheskoi Khimii) (1999), 35(5), 711-714  
CODEN: RJOCEQ; ISSN: 1070-4280

PUBLISHER:

MAIK Nauka/Interperiodica Publishing

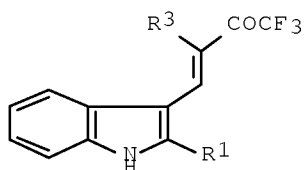
DOCUMENT TYPE:

Journal

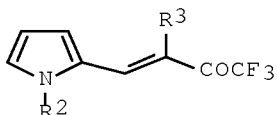
LANGUAGE:

English

GI



II



III

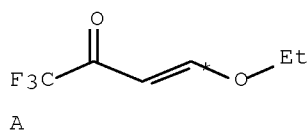
AB Indoles and pyrroles react with (E)-4-ethoxy-1,1,1-trifluoro-3-buten-2-one (I) and 3-(ethoxymethylene)-1,1,1,5,5,5-hexafluoro-2,4-pentanedione in the presence of  $\text{ZnCl}_2$  to give hetaryl-substituted enones II ( $\text{R}_1 = \text{Me}, \text{Ph}$ ;  $\text{R}_3 = \text{H}, \text{COCF}_3$ ) and III ( $\text{R}_2 = \text{H}, \text{Me}$ ;  $\text{R}_3 = \text{H}, \text{COCF}_3$ ) containing, resp., one or two trifluoroacetyl groups. The reactions with I are stereospecific, and only E isomers of the corresponding enones are formed.

REFERENCE COUNT:

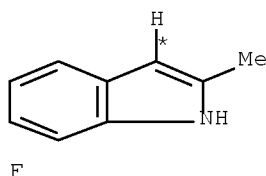
12

THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(2) OF 9 A + F ==> G

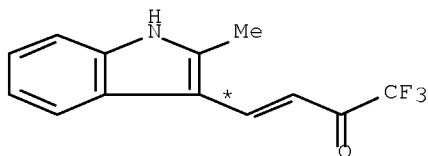


A



F

(2) →



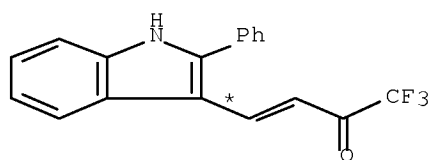
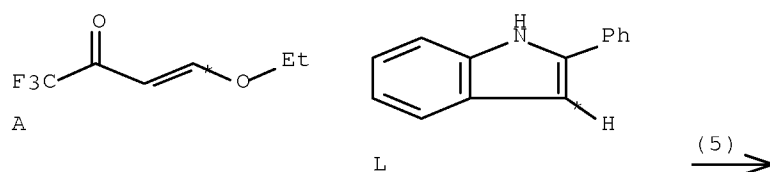
G  
YIELD 78%

RX(2) RCT A 59938-06-6, F 95-20-5  
RGT H 7646-85-7  $\text{ZnCl}_2$   
PRO G 202074-31-5

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SOL 75-09-2 CH2Cl2

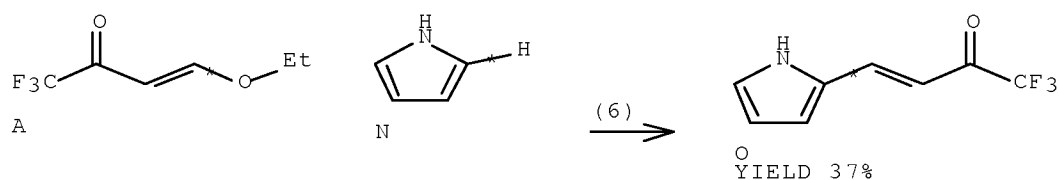
RX(5) OF 9 A + L ==> M



M  
YIELD 56%

RX(5) RCT A 59938-06-6, L 948-65-2  
 RGT H 7646-85-7 ZnCl2  
 PRO M 202074-32-6  
 SOL 75-09-2 CH2Cl2

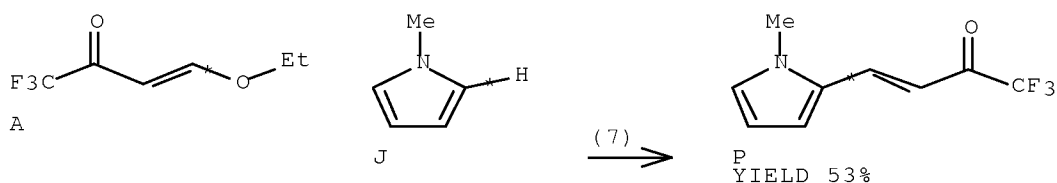
RX(6) OF 9 A + N ==> O



RX(6) RCT A 59938-06-6, N 109-97-7  
 RGT H 7646-85-7 ZnCl2  
 PRO O 202074-27-9  
 SOL 75-09-2 CH2Cl2

RX(7) OF 9 A + J ==> P

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RX(7) RCT A 59938-06-6, J 96-54-8  
RGT H 7646-85-7 ZnCl2  
PRO P 202074-28-0  
SOL 75-09-2 CH2Cl2

L46 ANSWER 11 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 129:216528 CASREACT [Full-text](#)

TITLE:  $\alpha$ -Vinylation of  $\beta$ -aminothiophene derivatives. synthesis of 6-functionalized thieno[3,2-b]pyridines

AUTHOR(S): Berkaoui, M'hamed; Outurquin, Francis; Paulmier, Claude

CORPORATE SOURCE: Laboratoire de Synthèse Thio et Selenoorganique, Université de Rouen, Mont-Saint-Aignan, F-76821, Fr.

SOURCE: Tetrahedron (1998), 54(31), 9055-9066  
CODEN: TETRAB; ISSN: 0040-4020

PUBLISHER: Elsevier Science Ltd.

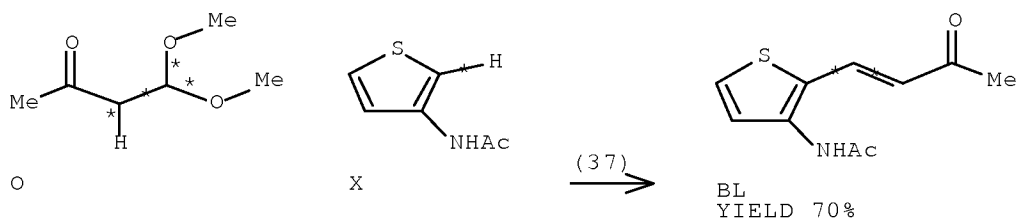
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The acid-catalyzed reductive  $\alpha$ -alkylation of  $\beta$ -aminothiophene derivs. was applied to the N-(3-thienyl)acetamide and alkyl N-(3-thienyl)carbamates. Without reduction,  $\beta$ -amino  $\alpha$ -vinylthiophenes were obtained when  $\alpha$ -branched aldehydes were used.  $\beta$ -(3-Amino-2-thienyl) $\alpha,\beta$ -unsatd. ketones, esters and nitriles were also prepared from the corresponding  $\alpha$ -functionalized acetals. These amines are intermediates in the formation of thieno[3,2-b]pyridines bearing a functional group at the  $\beta$ -position of the pyridine ring.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(37) OF 56 O + X ==> BL



RX(37) RCT O 5436-21-5, X 42602-67-5

10/569486

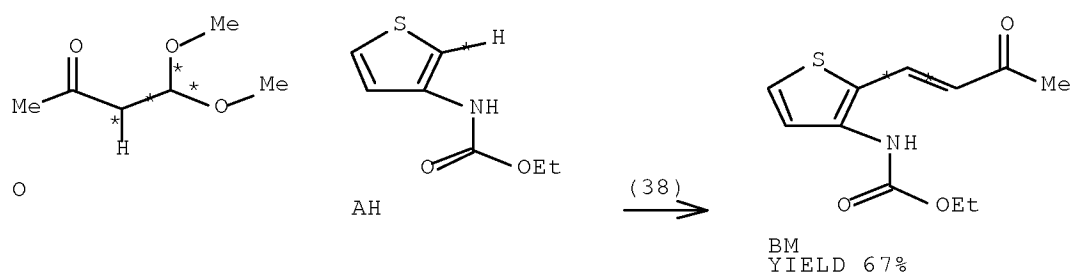
STAGE(1)  
SOL 75-09-2 CH2Cl2

STAGE(2)  
RGT D 7647-01-0 HCl

STAGE(3)  
RGT E 1310-73-2 NaOH

PRO BL 75877-30-4

RX(38) OF 56 O + AH ==> BM



RX(38) RCT O 5436-21-5, AH 701-93-9

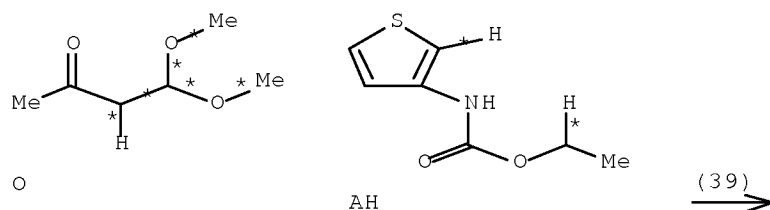
STAGE(1)  
SOL 75-09-2 CH2Cl2

STAGE(2)  
RGT D 7647-01-0 HCl

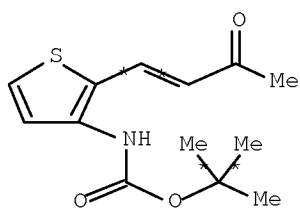
STAGE(3)  
RGT E 1310-73-2 NaOH

PRO BM 212570-81-5

RX(39) OF 56 O + AH ==> BA...



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BA  
YIELD 80%

RX(39) RCT O 5436-21-5, AH 701-93-9

STAGE(1)

SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

STAGE(2)

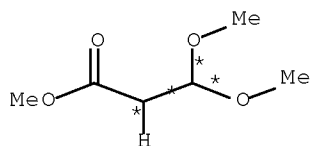
RGT D 7647-01-0 HCl

STAGE(3)

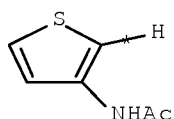
RGT E 1310-73-2 NaOH

PRO BA 212570-83-7

RX(40) OF 56 BI + X ==> BN

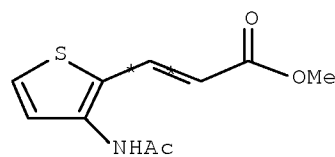


BI



X

(40)



BN  
YIELD 88%

RX(40) RCT BI 7424-91-1, X 42602-67-5

STAGE(1)

SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

STAGE(2)

RGT D 7647-01-0 HCl

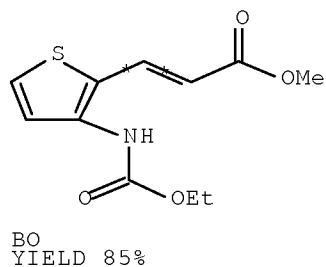
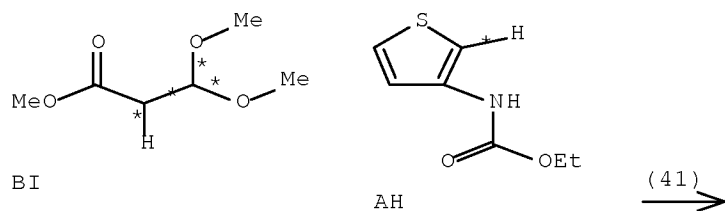
STAGE(3)

RGT E 1310-73-2 NaOH

PRO BN 75877-28-0

RX(41) OF 56 BI + AH ==> BO

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RX(41) RCT BI 7424-91-1, AH 701-93-9

STAGE(1)

SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

STAGE(2)

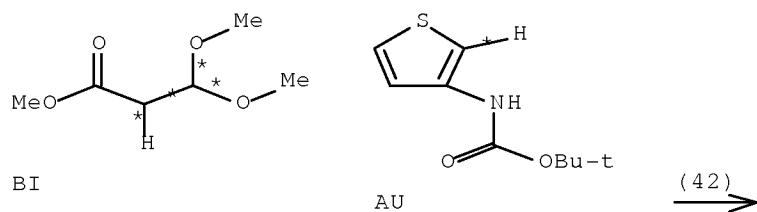
RGT D 7647-01-0 HCl

STAGE(3)

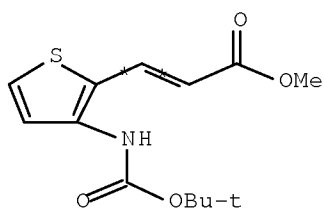
RGT E 1310-73-2 NaOH

PRO BO 212571-14-7

RX(42) OF 56 BI + AU ==> BE...



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BE  
YIELD 75%

RX(42) RCT BI 7424-91-1, AU 19228-91-2

STAGE(1)

SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

STAGE(2)

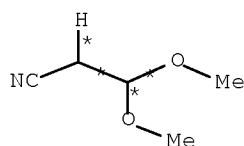
RGT D 7647-01-0 HCl

STAGE(3)

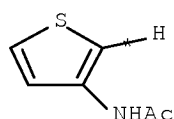
RGT E 1310-73-2 NaOH

PRO BE 212570-86-0

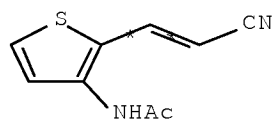
RX(43) OF 56 Q + X ==> BP



Q



X



BP  
YIELD 63%

RX(43) RCT Q 57597-62-3, X 42602-67-5

STAGE(1)

SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

STAGE(2)

RGT D 7647-01-0 HCl

STAGE(3)

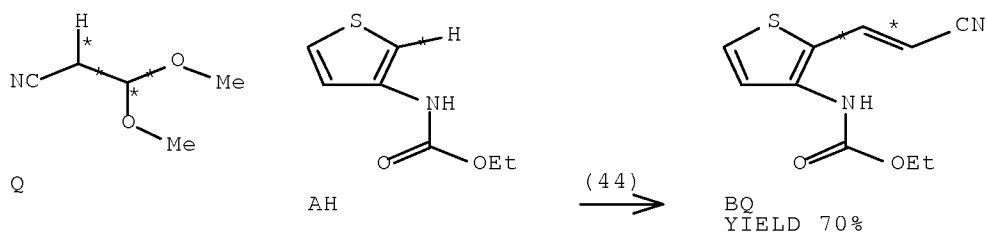
RGT E 1310-73-2 NaOH

PRO BP 212570-88-2

RX(44) OF 56 Q + AH ==> BQ



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RX(44) RCT Q 57597-62-3, AH 701-93-9

STAGE(1)

SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

STAGE(2)

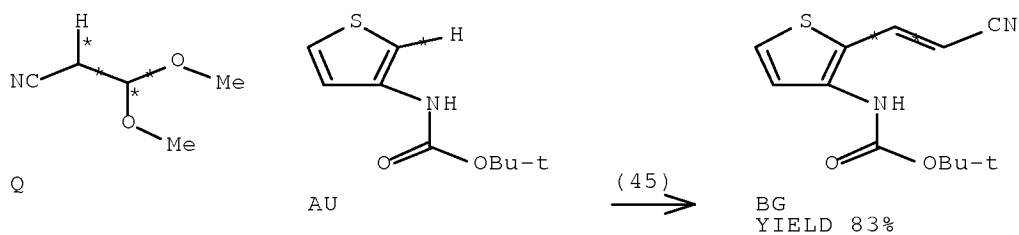
RGT D 7647-01-0 HCl

STAGE(3)

RGT E 1310-73-2 NaOH

PRO BQ 212570-90-6

RX(45) OF 56 Q + AU  $\implies$  BG...



RX(45) RCT Q 57597-62-3, AU 19228-91-2

STAGE(1)

SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

STAGE(2)

RGT D 7647-01-0 HCl

STAGE(3)

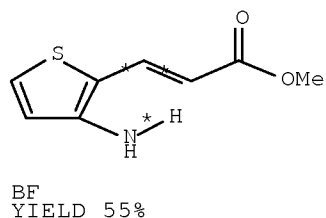
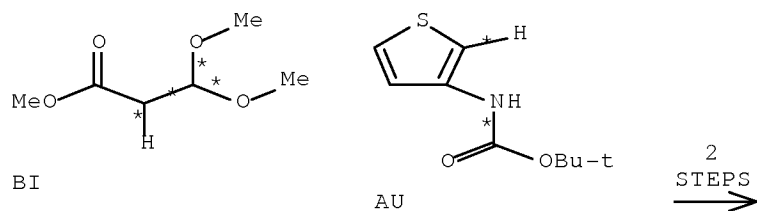
RGT E 1310-73-2 NaOH

PRO BG 212570-92-8

RX(51) OF 56 COMPOSED OF RX(42), RX(31)

RX(51) EI + AU  $\implies$  BF

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RX(42) RCT BI 7424-91-1, AU 19228-91-2

STAGE(1)

SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

STAGE(2)

RGT D 7647-01-0 HCl

STAGE(3)

RGT E 1310-73-2 NaOH

PRO BE 212570-86-0

RX(31) RCT BE 212570-86-0

STAGE(1)

RGT BC 10035-10-6 HBr, BD 64-19-7 AcOH

STAGE(2)

SOL 60-29-7 Et<sub>2</sub>O

STAGE(3)

SOL 7732-18-5 Water

STAGE(4)

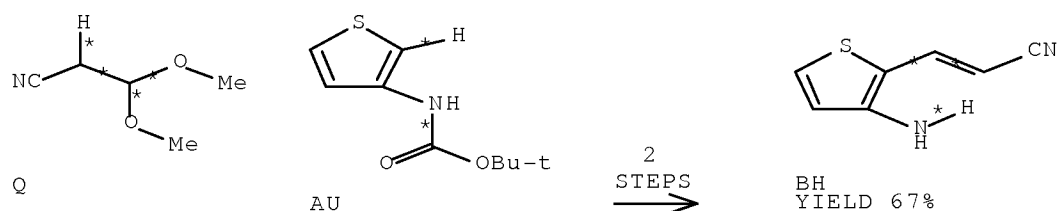
RGT E 1310-73-2 NaOH

PRO BF 75877-27-9

RX(52) OF 56 COMPOSED OF RX(45), RX(32)

RX(52) Q + AU ==> BH

10/569486



RX(45) RCT Q 57597-62-3, AU 19228-91-2

STAGE(1)

SOL 75-09-2 CH2Cl2

STAGE(2)

RGT D 7647-01-0 HCl

STAGE(3)

RGT E 1310-73-2 NaOH

PRO BG 212570-92-8

RX(32) RCT BG 212570-92-8

STAGE(1)

RGT BC 10035-10-6 HBr, BD 64-19-7 AcOH

STAGE(2)

RGT BB 60-29-7 Et2O

STAGE(3)

SOL 7732-18-5 Water

STAGE(4)

RGT E 1310-73-2 NaOH

PRO BH 212570-96-2

L46 ANSWER 12 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 125:329061 CASREACT [Full-text](#)

TITLE: Reactions of endocyclic linearly conjugated dienolates with Michael acceptors leading to bicyclo[2.2.2]octane derivatives. Application to the synthesis of C13 degradation products of carotenoids

AUTHOR(S): Ito, Nobuhiko; Etoh, Takeaki

CORPORATE SOURCE: Research Development Lab., Soda Aromatic Co., Ltd., Noda, 270-02, Japan

SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1996), (19), 2397-2405

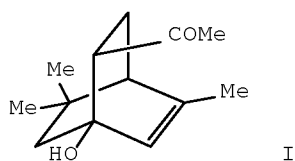
CODEN: JCPRB4; ISSN: 0300-922X

PUBLISHER: Royal Society of Chemistry

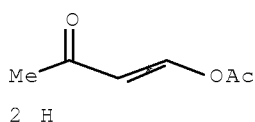
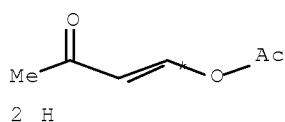
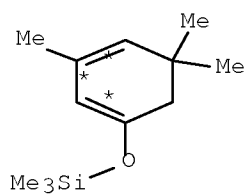
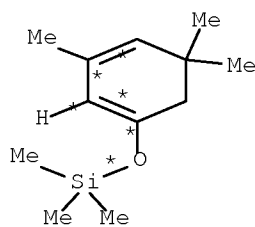
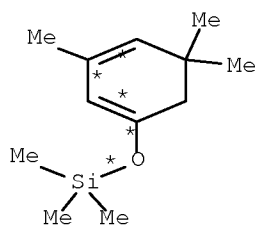
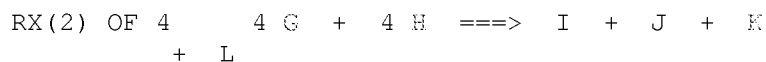
DOCUMENT TYPE: Journal

LANGUAGE: English

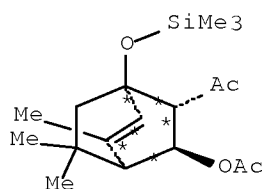
GI



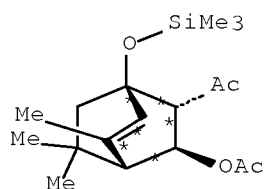
AB The endocyclic linearly conjugated dienolates from substituted cyclohex-2-enones react with but-3-en-2-one, substituted Me propenoates, but-3-yn-2-one and Me propiolate to afford bicyclo[2.2.2]oct-2-en-1-ols, e.g. I, and bicyclo[2.2.2]octa-2,5-dien-1-ols. The  $\text{AlCl}_3$ -catalyzed reaction of 3,5,5-trimethyl-1-(trimethylsiloxy)cyclohexa-1,3-diene with (E)-4-acetoxy- and (E)-4-methoxybut-3-en-2-one provides trans-8-acetoxy-7-acetyl-3,5,5-trimethyl-1-(trimethylsiloxy)bicyclo[2.2.2]oct-2-enes and trans-7-acetyl-8-methoxy-3,5,5-trimethyl-1-(trimethylsiloxy)bicyclo[2.2.2]oct-2-enes. Starting from these bicyclo[2.2.2]octenes, the  $\text{Cl}_3$  degradation products of carotenoids including 3-oxo-a-ionone, blumenol-C and 1,3,7,7-tetramethyl-2-oxabicyclo[4.4.0]decan-9-one have been synthesized.



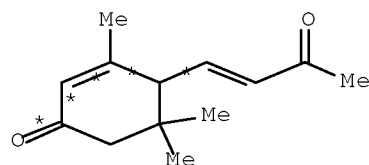
10/569486



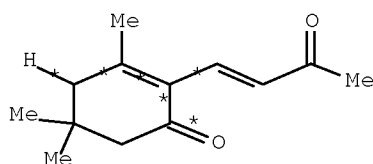
I  
YIELD 13%



J  
YIELD 15%



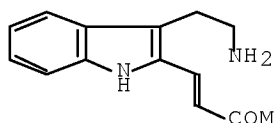
K  
YIELD 30%



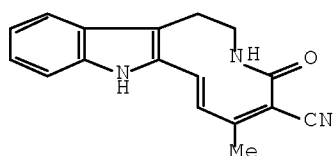
L  
YIELD 10%

RX(2) RCT G 80699-65-6, H 51731-15-8  
RGT M 7446-70-0 AlCl3  
PRO I 141915-26-6, J 141979-75-1, K 79734-43-3, L  
183282-14-6  
SOL 75-09-2 CH2Cl2

L46 ANSWER 13 OF 24 CASREACT COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 121:133898 CASREACT [Full-text](#)  
TITLE: Synthesis of heterocyclic compounds with  
hydroxymethylene ketones. XIV. Contribution to the  
regioselectivity of the reaction of acetoacetaldehyde  
with tryptamine  
AUTHOR(S): Teuber, Hans-Joachim; Quintanilla-Licea, Ramiro  
CORPORATE SOURCE: Inst. fuer Organische Chemie, J.W. Goethe-Univ.,  
Frankfurt/Main, Germany  
SOURCE: Journal fuer Praktische Chemie/Chemiker-Zeitung  
(1994), 336(5), 452-7  
CODEN: JPCCEM; ISSN: 0941-1216  
DOCUMENT TYPE: Journal  
LANGUAGE: German  
GI



I

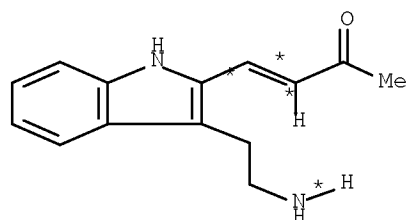
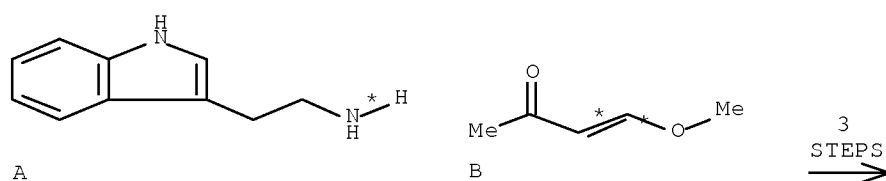


II

AB The range of substitution products of tryptamine with acetoacetaldehyde as substituent at the basic or the indole nitrogen is completed by a product I containing the substituent in the indole  $\alpha$ -position. I is formed by ring opening of 1,2,3,4-tetrahydro-1-(2-oxopropyl)- $\beta$ -carboline. The synthesis of the azocinoindole II is described. Reaction conditions are described and the  $^1\text{H-NMR}$  spectra comparatively discussed.

RX(10) OF 13 COMPOSED OF RX(1), RX(2), RX(3)

RX(10) A + B ==> I



I  
YIELD 41%

RX(1)	RCT	A 61-54-1, B 4652-27-1
	PRO	C 157103-24-7
	SOL	75-09-2 CH <sub>2</sub> Cl <sub>2</sub>
RX(2)	RCT	C 157103-24-7
	RGT	F 7647-01-0 HCl
	PRO	E 157103-26-9
	SOL	7732-18-5 Water, 67-56-1 MeOH
RX(3)	RCT	E 157103-26-9
	PRO	I 157103-27-0
	SOL	7732-18-5 Water, 67-56-1 MeOH
	NTE	thermal

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L46 ANSWER 14 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 118:39323 CASREACT Full-text

TITLE: Synthesis of carbocyclic nucleosides: synthesis of  
(±)-2,2-bis(hydroxymethyl)cyclopropyl nucleosides  
AUTHOR(S): Izawa, Takao; Nishiyama, Shigeru; Yamamura, Shoshuke;  
Kato, Kuniki; Takita, Tomohisa

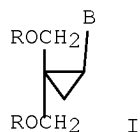
CORPORATE SOURCE: Fac. Sci. Technol., Keio Univ., Hiyoshi, 223, Japan  
SOURCE: Journal of the Chemical Society, Perkin Transactions  
1: Organic and Bio-Organic Chemistry (1972-1999)  
(1992), (19), 2519-25

CODEN: JCPRB4; ISSN: 0300-922X

DOCUMENT TYPE: Journal

LANGUAGE: English

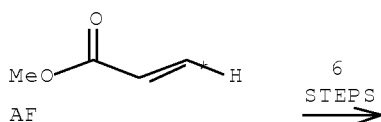
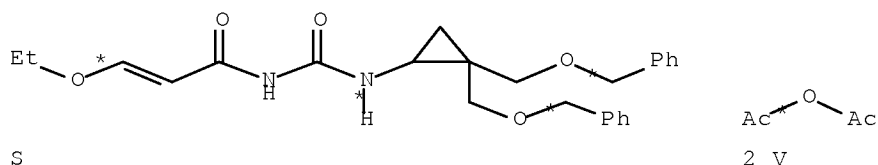
GI



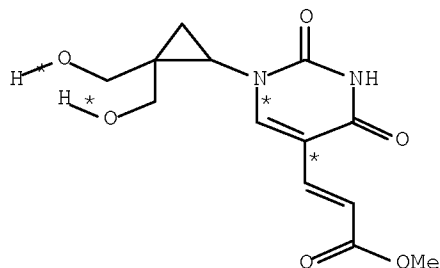
AB Treatment of cyclopropanecarboxylic acid I (R = CH<sub>2</sub>Ph, B = CO<sub>2</sub>H) with Et chloroformate and NaN<sub>3</sub> followed by thermolysis of the resulting keto azide I (B = CON<sub>3</sub>) at 80° provided the corresponding isocyanate I (B = NCO), which was then converted into I (B = NH<sub>2</sub>, NHCONH<sub>2</sub>) (II). The racemic 2,2-bis(hydroxymethyl)cyclopropylpyrimidine nucleosides, e.g. I (R = H, B = adenine, guanine, thymine, uracil), were prepared from II. None of the carbocyclic nucleosides showed any significant anti-HIV activity.

RX(155) OF 201 COMPOSED OF RX(9), RX(10), RX(11), RX(13), RX(15), RX(16)

RX(155) S + 2 V + AF ==> AG



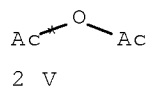
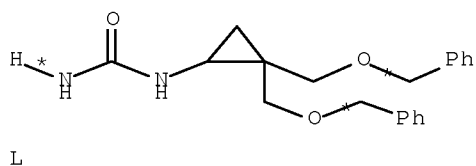
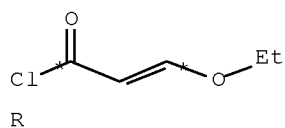
10/569486



AG

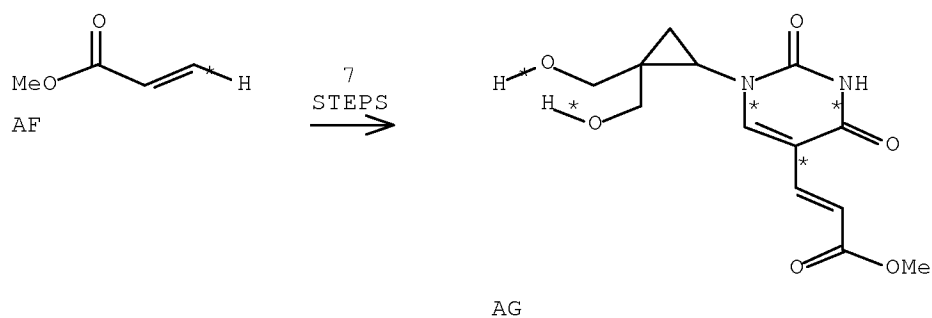
RX(9)	RCT	S	135345-90-3
	RGT	M	7664-41-7 NH3
	PRO	T	135345-91-4
RX(10)	RCT	T	135345-91-4
	PRO	U	135345-83-4
	NTE		H2/PD
RX(11)	RCT	U	135345-83-4, V 108-24-7
	PRO	W	145215-09-4
RX(13)	RCT	W	145215-09-4
	RGT	AA	10377-51-2 LiI
	PRO	Z	145215-11-8
	NTE		(NH4)2[CE(NO3)6]
RX(15)	RCT	Z	145215-11-8
	RGT	AC	124-41-4 NaOMe
	PRO	AE	145215-14-1
	SOL		67-56-1 MeOH
RX(16)	RCT	AF	96-33-3, AE 145215-14-1
	RGT	AH	603-35-0 PPh3
	PRO	AG	145215-18-5
	CAT		3375-31-3 Pd(OAc)2

RX(157) OF 201 COMPOSED OF RX(8), RX(9), RX(10), RX(11), RX(13), RX(15), RX(16)  
 RX(157) R + L + 2 V + AF ==> AG





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RX(8) RCT R 99471-66-6, L 135345-89-0  
PRO S 135345-90-3

RX(9) RCT S 135345-90-3  
RGT M 7664-41-7 NH3  
PRO T 135345-91-4

RX(10) RCT T 135345-91-4  
PRO U 135345-83-4  
NTE H2/PD

RX(11) RCT U 135345-83-4, V 108-24-7  
PRO W 145215-09-4

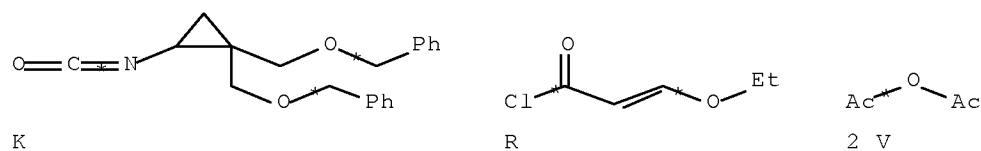
RX(13) RCT W 145215-09-4  
RGT AA 10377-51-2 LiI  
PRO Z 145215-11-8  
NTE (NH4)2[CE(NO3)6]

RX(15) RCT Z 145215-11-8  
RGT AC 124-41-4 NaOMe  
PRO AE 145215-14-1  
SOL 67-56-1 MeOH

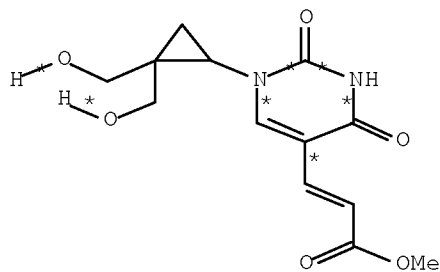
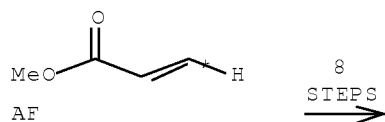
RX(16) RCT AF 96-33-3, AE 145215-14-1  
RGT AH 603-35-0 PPh3  
PRO AG 145215-18-5  
CAT 3375-31-3 Pd(OAc)2

RX(159) OF 201 COMPOSED OF RX(5), RX(8), RX(9), RX(10), RX(11), RX(13), RX(15),  
RX(16)

RX(159) K + R + 2 V + AF ==> AG



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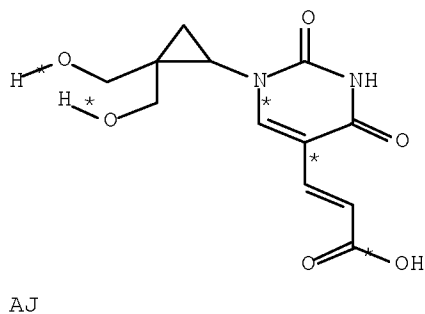
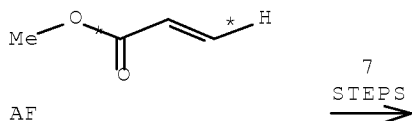
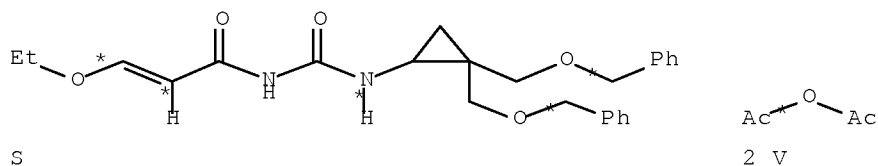
AG

RX(5)	RCT	K	135345-85-6
	RGT	M	7664-41-7 NH3
	PRO	L	135345-89-0
RX(8)	RCT	R	99471-66-6, L 135345-89-0
	PRO	S	135345-90-3
RX(9)	RCT	S	135345-90-3
	RGT	M	7664-41-7 NH3
	PRO	T	135345-91-4
RX(10)	RCT	T	135345-91-4
	PRO	U	135345-83-4
	NTE		H2/PD
RX(11)	RCT	U	135345-83-4, V 108-24-7
	PRO	W	145215-09-4
RX(13)	RCT	W	145215-09-4
	RGT	AA	10377-51-2 LiI
	PRO	Z	145215-11-8
	NTE		(NH4)2[CE(NO3)6]
RX(15)	RCT	Z	145215-11-8
	RGT	AC	124-41-4 NaOMe
	PRO	AE	145215-14-1
	SOL		67-56-1 MeOH
RX(16)	RCT	AF	96-33-3, AE 145215-14-1
	RGT	AH	603-35-0 PPh3
	PRO	AG	145215-18-5
	CAT		3375-31-3 Pd(OAc)2

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RX(165) OF 201 COMPOSED OF RX(9), RX(10), RX(11), RX(13), RX(15), RX(16),  
RX(17)

RX(165) S + 2 V + AF ==> AJ



RX(9)	RCT	S	135345-90-3
	RGT	M	7664-41-7 NH3
	PRO	T	135345-91-4
RX(10)	RCT	T	135345-91-4
	PRO	U	135345-83-4
	NTE		H2/PD
RX(11)	RCT	U	135345-83-4, V 108-24-7
	PRO	W	145215-09-4
RX(13)	RCT	W	145215-09-4
	RGT	AA	10377-51-2 LiI
	PRO	Z	145215-11-8
	NTE		(NH4)2 [CE(NO3)6]
RX(15)	RCT	Z	145215-11-8
	RGT	AC	124-41-4 NaOMe
	PRO	AE	145215-14-1

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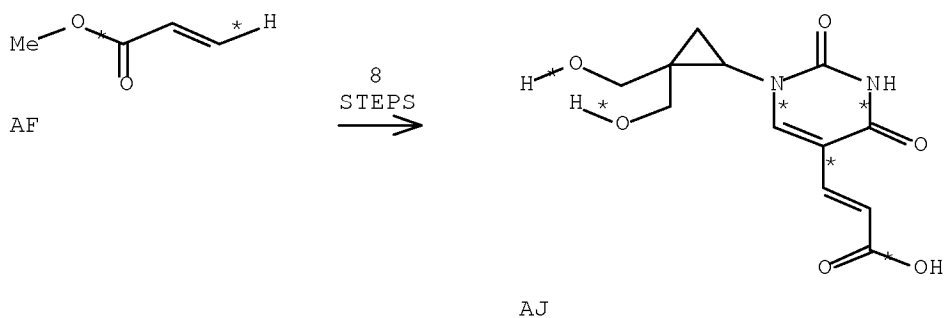
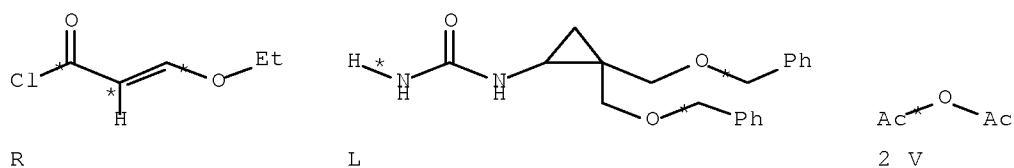
SOL 67-56-1 MeOH

RX(16) RCT AF 96-33-3, AE 145215-14-1  
 RGT AH 603-35-0 PPh3  
 PRO AG 145215-18-5  
 CAT 3375-31-3 Pd(OAc)2

RX(17) RCT AG 145215-18-5  
 RGT AK 1310-73-2 NaOH  
 PRO AJ 145215-19-6

RX(167) OF 201 COMPOSED OF RX(8), RX(9), RX(10), RX(11), RX(13), RX(15),  
 RX(16), RX(17)

RX(167) R + L + 2 V + AF ==> AJ



RX(8) RCT R 99471-66-6, L 135345-89-0  
 PRO S 135345-90-3

RX(9) RCT S 135345-90-3  
 RGT M 7664-41-7 NH3  
 PRO T 135345-91-4

RX(10) RCT T 135345-91-4  
 PRO U 135345-83-4  
 NTE H2/PD

RX(11) RCT U 135345-83-4, V 108-24-7  
 PRO W 145215-09-4

RX(13) RCT W 145215-09-4  
 RGT AA 10377-51-2 LiI

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PRO Z 145215-11-8  
NTE (NH<sub>4</sub>)<sub>2</sub> [CE(NO<sub>3</sub>)<sub>6</sub>]

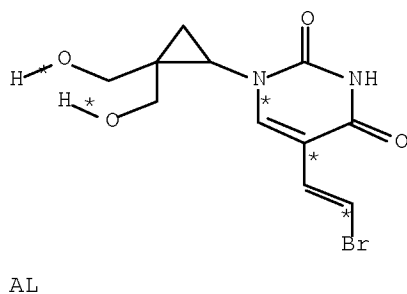
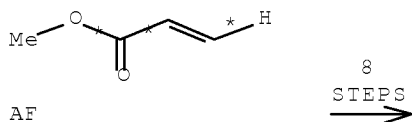
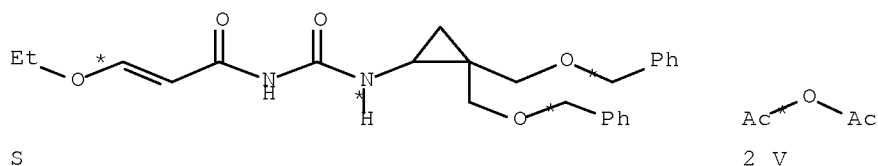
RX(15) RCT Z 145215-11-8  
RGT AC 124-41-4 NaOMe  
PRO AE 145215-14-1  
SOL 67-56-1 MeOH

RX(16) RCT AF 96-33-3, AE 145215-14-1  
RGT AH 603-35-0 PPh<sub>3</sub>  
PRO AG 145215-18-5  
CAT 3375-31-3 Pd(OAc)<sub>2</sub>

RX(17) RCT AG 145215-18-5  
RGT AK 1310-73-2 NaOH  
PRO AJ 145215-19-6

RX(175) OF 201 COMPOSED OF RX(9), RX(10), RX(11), RX(13), RX(15), RX(16),  
RX(17), RX(18)

RX(175) S + 2 V + AF ==> AL



RX(9) RCT S 135345-90-3  
RGT M 7664-41-7 NH<sub>3</sub>

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PRO T 135345-91-4

RX(10) RCT T 135345-91-4  
PRO U 135345-83-4  
NTE H2/PD

RX(11) RCT U 135345-83-4, V 108-24-7  
PRO W 145215-09-4

RX(13) RCT W 145215-09-4  
RGT AA 10377-51-2 LiI  
PRO Z 145215-11-8  
NTE (NH4)2[CE(NO3)6]

RX(15) RCT Z 145215-11-8  
RGT AC 124-41-4 NaOMe  
PRO AE 145215-14-1  
SOL 67-56-1 MeOH

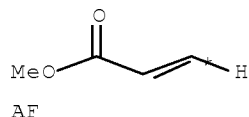
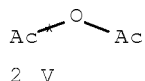
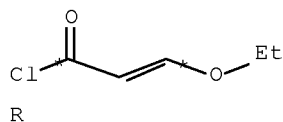
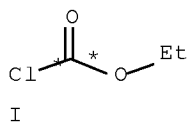
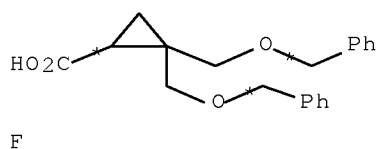
RX(16) RCT AF 96-33-3, AE 145215-14-1  
RGT AH 603-35-0 PPh3  
PRO AG 145215-18-5  
CAT 3375-31-3 Pd(OAc)2

RX(17) RCT AG 145215-18-5  
RGT AK 1310-73-2 NaOH  
PRO AJ 145215-19-6

RX(18) RCT AJ 145215-19-6  
RGT AM 128-08-5 Bromosuccinimide  
PRO AL 145215-20-9

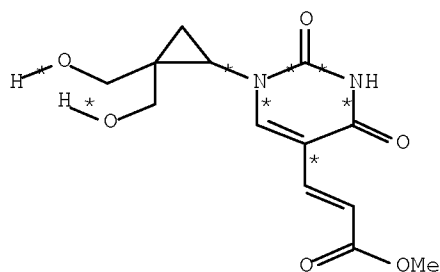
RX(184) OF 201 COMPOSED OF RX(4), RX(5), RX(8), RX(9), RX(10), RX(11), RX(13),  
RX(15), RX(16)

RX(184) F + I + R + 2 V + AF ==> AG



9  
STEPS  
→

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AG

RX(4) RCT F 135345-84-5, I 541-41-3  
 RGT J 26628-22-8 NaN3  
 PRO K 135345-85-6

RX(5) RCT K 135345-85-6  
 RGT M 7664-41-7 NH3  
 PRO L 135345-89-0

RX(8) RCT R 99471-66-6, L 135345-89-0  
 PRO S 135345-90-3

RX(9) RCT S 135345-90-3  
 RGT M 7664-41-7 NH3  
 PRO T 135345-91-4

RX(10) RCT T 135345-91-4  
 PRO U 135345-83-4  
 NTE H2/PD

RX(11) RCT U 135345-83-4, V 108-24-7  
 PRO W 145215-09-4

RX(13) RCT W 145215-09-4  
 RGT AA 10377-51-2 LiI  
 PRO Z 145215-11-8  
 NTE (NH4)2[CE(NO3)6]

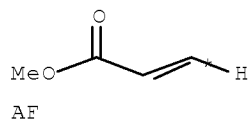
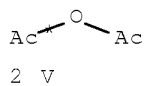
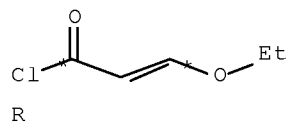
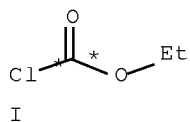
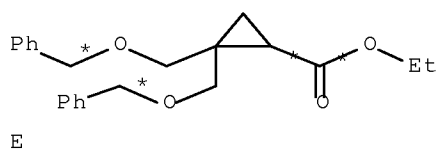
RX(15) RCT Z 145215-11-8  
 RGT AC 124-41-4 NaOMe  
 PRO AE 145215-14-1  
 SOL 67-56-1 MeOH

RX(16) RCT AF 96-33-3, AE 145215-14-1  
 RGT AH 603-35-0 PPh3  
 PRO AG 145215-18-5  
 CAT 3375-31-3 Pd(OAc)2

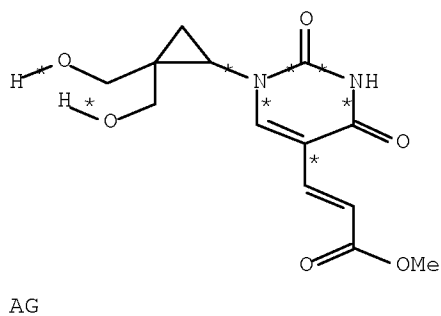
RX(186) OF 201 COMPOSED OF RX(2), RX(4), RX(5), RX(8), RX(9), RX(10), RX(11),  
 RX(13), RX(15), RX(16)

RX(186) E + I + R + 2 V + AF ==> AG

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10  
STEPS  
→



RX(2)	RCT	E	145215-00-5
	RGT	G	1310-58-3 KOH
	PRO	F	135345-84-5
RX(4)	RCT	F	135345-84-5, I 541-41-3
	RGT	J	26628-22-8 NaN3
	PRO	K	135345-85-6
RX(5)	RCT	K	135345-85-6
	RGT	M	7664-41-7 NH3
	PRO	L	135345-89-0
RX(8)	RCT	R	99471-66-6, L 135345-89-0
	PRO	S	135345-90-3
RX(9)	RCT	S	135345-90-3
	RGT	M	7664-41-7 NH3
	PRO	T	135345-91-4
RX(10)	RCT	T	135345-91-4
	PRO	U	135345-83-4
	NTE		H2/PD
RX(11)	RCT	U	135345-83-4, V 108-24-7



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PRO W 145215-09-4

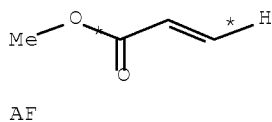
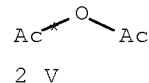
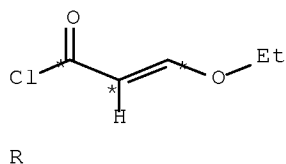
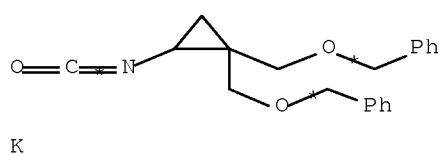
RX(13) RCT W 145215-09-4  
RGT AA 10377-51-2 LiI  
PRO Z 145215-11-8  
NTE (NH4)2[CE(NO3)6]

RX(15) RCT Z 145215-11-8  
RGT AC 124-41-4 NaOMe  
PRO AE 145215-14-1  
SOL 67-56-1 MeOH

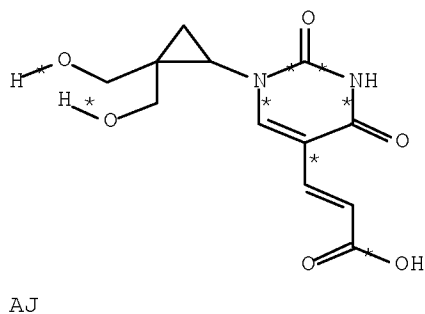
RX(16) RCT AF 96-33-3, AE 145215-14-1  
RGT AH 603-35-0 PPh3  
PRO AG 145215-18-5  
CAT 3375-31-3 Pd(OAc)2

RX(188) OF 201 COMPOSED OF RX(5), RX(8), RX(9), RX(10), RX(11), RX(13), RX(15),  
RX(16), RX(17)

RX(188) K + R + 2 V + AF ==> AJ



9  
STEPS  
→



RX(5) RCT K 135345-85-6  
RGT M 7664-41-7 NH3

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PRO L 135345-89-0

RX(8) RCT R 99471-66-6, L 135345-89-0  
PRO S 135345-90-3

RX(9) RCT S 135345-90-3  
RGT M 7664-41-7 NH3  
PRO T 135345-91-4

RX(10) RCT T 135345-91-4  
PRO U 135345-83-4  
NTE H2/PD

RX(11) RCT U 135345-83-4, V 108-24-7  
PRO W 145215-09-4

RX(13) RCT W 145215-09-4  
RGT AA 10377-51-2 LiI  
PRO Z 145215-11-8  
NTE (NH4)2[CE(NO3)6]

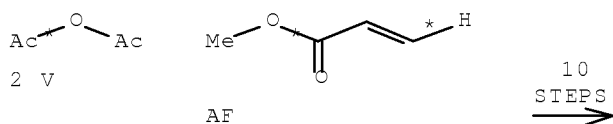
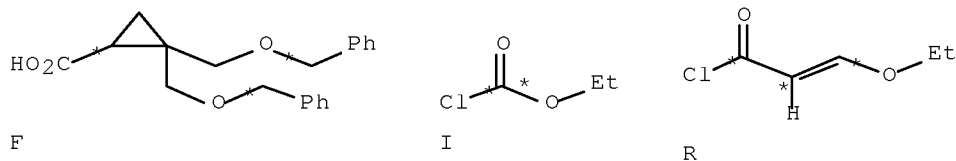
RX(15) RCT Z 145215-11-8  
RGT AC 124-41-4 NaOMe  
PRO AE 145215-14-1  
SOL 67-56-1 MeOH

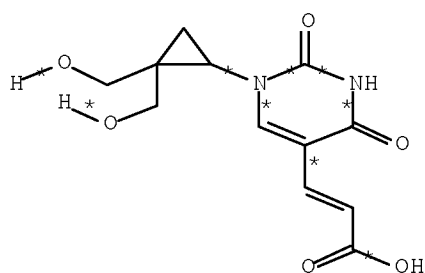
RX(16) RCT AF 96-33-3, AE 145215-14-1  
RGT AH 603-35-0 PPh3  
PRO AG 145215-18-5  
CAT 3375-31-3 Pd(OAc)2

RX(17) RCT AG 145215-18-5  
RGT AK 1310-73-2 NaOH  
PRO AJ 145215-19-6

RX(190) OF 201 COMPOSED OF RX(4), RX(5), RX(8), RX(9), RX(10), RX(11), RX(13),  
RX(15), RX(16), RX(17)

RX(190) F + I + R + 2 V + AF ==> AJ





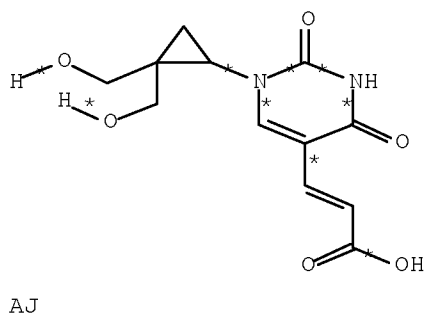
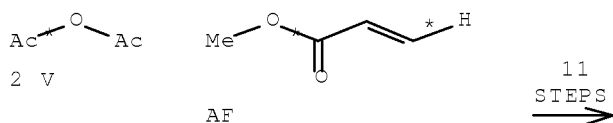
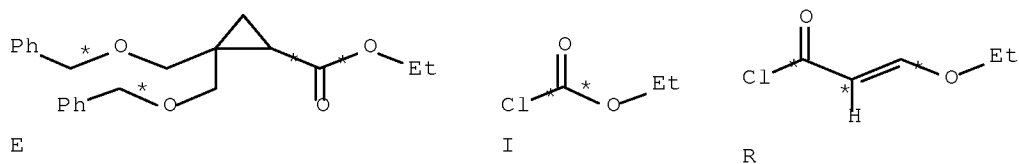
AJ

RX(4)	RCT	F	<del>135345-84-5</del> , I 541-41-3
	RGT	J	26628-22-8 NaN <sub>3</sub>
	PRO	K	135345-85-6
RX(5)	RCT	K	135345-85-6
	RGT	M	7664-41-7 NH <sub>3</sub>
	PRO	L	135345-89-0
RX(8)	RCT	R	<del>99471-66-6</del> , L 135345-89-0
	PRO	S	135345-90-3
RX(9)	RCT	S	135345-90-3
	RGT	M	7664-41-7 NH <sub>3</sub>
	PRO	T	135345-91-4
RX(10)	RCT	T	135345-91-4
	PRO	U	135345-83-4
	NTE		H <sub>2</sub> /PD
RX(11)	RCT	U	135345-83-4, V 108-24-7
	PRO	W	145215-09-4
RX(13)	RCT	W	145215-09-4
	RGT	AA	<del>10377-51-2</del> LiI
	PRO	Z	145215-11-8
	NTE		(NH <sub>4</sub> ) <sub>2</sub> [CE(NO <sub>3</sub> ) <sub>6</sub> ]
RX(15)	RCT	Z	145215-11-8
	RGT	AC	124-41-4 NaOMe
	PRO	AE	145215-14-1
	SOL		67-56-1 MeOH
RX(16)	RCT	AF	96-33-3, AE 145215-14-1
	RGT	AH	603-35-0 PPh <sub>3</sub>
	PRO	AG	145215-18-5
	CAT		3375-31-3 Pd(OAc) <sub>2</sub>
RX(17)	RCT	AG	145215-18-5
	RGT	AK	1310-73-2 NaOH
	PRO	AJ	<del>145215-19-6</del>

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RX(192) OF 201 COMPOSED OF RX(2), RX(4), RX(5), RX(8), RX(9), RX(10), RX(11),  
RX(13), RX(15), RX(16), RX(17)

RX(192) E + I + R + 2 V + AF ==> AJ



RX(2) RCT E 145215-00-5  
RGT G 1310-58-3 KOH  
PRO F 135345-84-5

RX(4) RCT F 135345-84-5, I 541-41-3  
RGT J 26628-22-8 NaN<sub>3</sub>  
PRO K 135345-85-6

RX(5) RCT K 135345-85-6  
RGT M 7664-41-7 NH<sub>3</sub>  
PRO L 135345-89-0

RX(8) RCT R 99471-66-6, L 135345-89-0  
PRO S 135345-90-3

RX(9) RCT S 135345-90-3  
RGT M 7664-41-7 NH<sub>3</sub>  
PRO T 135345-91-4

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RX(10) RCT T 135345-91-4  
 PRO U 135345-83-4  
 NTE H2/PD

RX(11) RCT U 135345-83-4, V 108-24-7  
 PRO W 145215-09-4

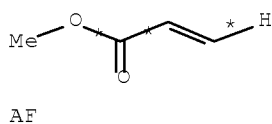
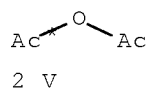
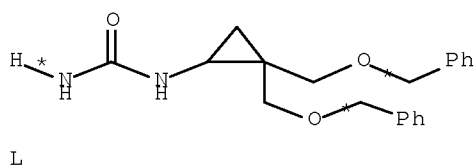
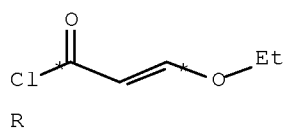
RX(13) RCT W 145215-09-4  
 RGT AA 10377-51-2 LiI  
 PRO Z 145215-11-8  
 NTE (NH4)2[CE(NO3)6]

RX(15) RCT Z 145215-11-8  
 RGT AC 124-41-4 NaOMe  
 PRO AE 145215-14-1  
 SOL 67-56-1 MeOH

RX(16) RCT AF 96-33-3, AE 145215-14-1  
 RGT AH 603-35-0 PPh3  
 PRO AG 145215-18-5  
 CAT 3375-31-3 Pd(OAc)2

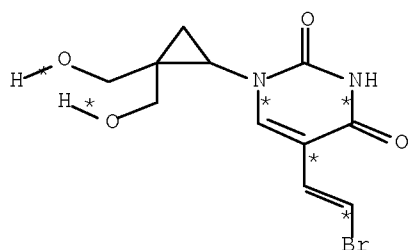
RX(17) RCT AG 145215-18-5  
 RGT AK 1310-73-2 NaOH  
 PRO AJ 145215-19-6

RX(194) OF 201 COMPOSED OF RX(8), RX(9), RX(10), RX(11), RX(13), RX(15),  
 RX(16), RX(17), RX(18)  
 RX(194) R + L + 2 V + AF ==> AL



9  
 STEPS  


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AL

RX(8) RCT R 99471-66-6, L 135345-89-0  
PRO S 135345-90-3

RX(9) RCT S 135345-90-3  
RGT M 7664-41-7 NH3  
PRO T 135345-91-4

RX(10) RCT T 135345-91-4  
PRO U 135345-83-4  
NTE H2/PD

RX(11) RCT U 135345-83-4, V 108-24-7  
PRO W 145215-09-4

RX(13) RCT W 145215-09-4  
RGT AA 10377-51-2 LiI  
PRO Z 145215-11-8  
NTE (NH4)2[CE(NO3)6]

RX(15) RCT Z 145215-11-8  
RGT AC 124-41-4 NaOMe  
PRO AE 145215-14-1  
SOL 67-56-1 MeOH

RX(16) RCT AF 96-33-3, AE 145215-14-1  
RGT AH 603-35-0 PPh3  
PRO AG 145215-18-5  
CAT 3375-31-3 Pd(OAc)2

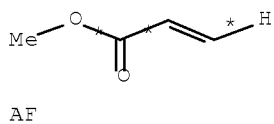
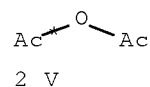
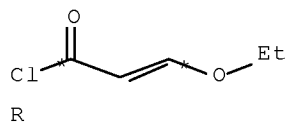
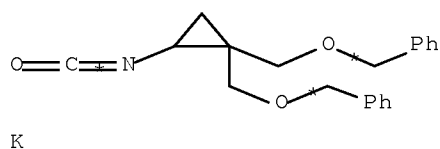
RX(17) RCT AG 145215-18-5  
RGT AK 1310-73-2 NaOH  
PRO AJ 145215-19-6

RX(18) RCT AJ 145215-19-6  
RGT AM 128-08-5 Bromosuccinimide  
PRO AL 145215-20-9

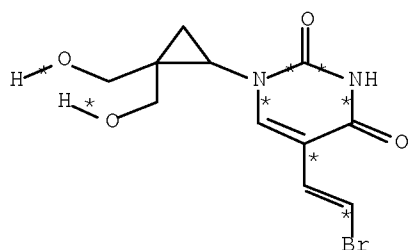
RX(196) OF 201 COMPOSED OF RX(5), RX(8), RX(9), RX(10), RX(11), RX(13), RX(15),  
RX(16), RX(17), RX(18)

RX(196) K + R + 2 V + AF ==> AL

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10  
STEPS  
→



RX(5)	RCT	K	135345-85-6
	RGT	M	7664-41-7 NH3
	PRO	L	135345-89-0
RX(8)	RCT	R	99471-66-6, L 135345-89-0
	PRO	S	135345-90-3
RX(9)	RCT	S	135345-90-3
	RGT	M	7664-41-7 NH3
	PRO	T	135345-91-4
RX(10)	RCT	T	135345-91-4
	PRO	U	135345-83-4
	NTE		H2/PD
RX(11)	RCT	U	135345-83-4, V 108-24-7
	PRO	W	145215-09-4
RX(13)	RCT	W	145215-09-4
	RGT	AA	10377-51-2 LiI
	PRO	Z	145215-11-8
	NTE		(NH4)2[CE(NO3)6]
RX(15)	RCT	Z	145215-11-8
	RGT	AC	124-41-4 NaOMe

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PRO AE 145215-14-1  
SOL 67-56-1 MeOH

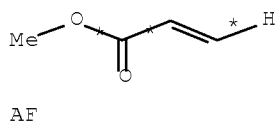
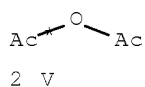
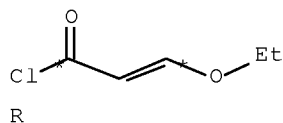
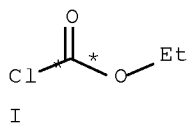
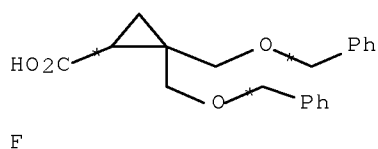
RX(16) RCT AF 96-33-3, AE 145215-14-1  
RGT AH 603-35-0 PPh3  
PRO AG 145215-18-5  
CAT 3375-31-3 Pd(OAc)2

RX(17) RCT AG 145215-18-5  
RGT AK 1310-73-2 NaOH  
PRO AJ 145215-19-6

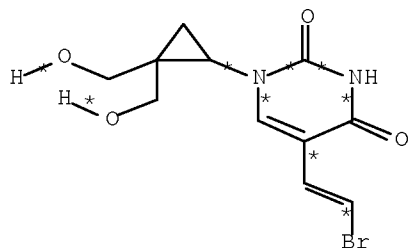
RX(18) RCT AJ 145215-19-6  
RGT AM 128-08-5 Bromosuccinimide  
PRO AL 145215-20-9

RX(198) OF 201 COMPOSED OF RX(4), RX(5), RX(8), RX(9), RX(10), RX(11), RX(13),  
RX(15), RX(16), RX(17), RX(18)

RX(198) F + I + R + 2 V + AF ==> AL



11  
STEPS  
→



RX(4) RCT F 135345-84-5, I 541-41-3  
RGT J 26628-22-8 NaN3  
PRO K 135345-85-6



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RX(5) RCT K 135345-85-6  
 RGT M 7664-41-7 NH3  
 PRO L 135345-89-0

RX(8) RCT R 99471-66-6, L 135345-89-0  
 PRO S 135345-90-3

RX(9) RCT S 135345-90-3  
 RGT M 7664-41-7 NH3  
 PRO T 135345-91-4

RX(10) RCT T 135345-91-4  
 PRO U 135345-83-4  
 NTE H2/PD

RX(11) RCT U 135345-83-4, V 108-24-7  
 PRO W 145215-09-4

RX(13) RCT W 145215-09-4  
 RGT AA 10377-51-2 LiI  
 PRO Z 145215-11-8  
 NTE (NH4)2[CE(NO3)6]

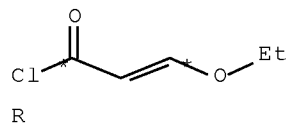
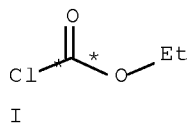
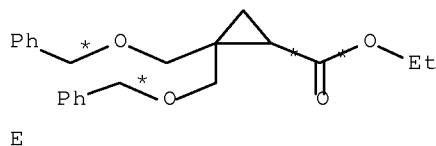
RX(15) RCT Z 145215-11-8  
 RGT AC 124-41-4 NaOMe  
 PRO AE 145215-14-1  
 SOL 67-56-1 MeOH

RX(16) RCT AF 96-33-3, AE 145215-14-1  
 RGT AH 603-35-0 PPh3  
 PRO AG 145215-18-5  
 CAT 3375-31-3 Pd(OAc)2

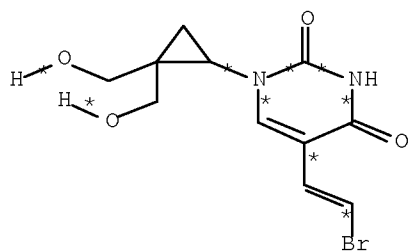
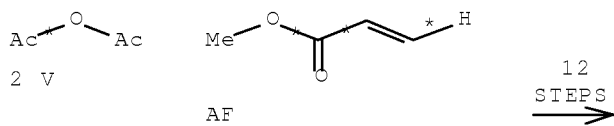
RX(17) RCT AG 145215-18-5  
 RGT AK 1310-73-2 NaOH  
 PRO AJ 145215-19-6

RX(18) RCT AJ 145215-19-6  
 RGT AM 128-08-5 Bromosuccinimide  
 PRO AL 145215-20-9

RX(200) OF 201 COMPOSED OF RX(2), RX(4), RX(5), RX(8), RX(9), RX(10), RX(11),  
 RX(13), RX(15), RX(16), RX(17), RX(18)  
 RX(200) E + I + R + 2 V + AF ==> AL



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AL

RX(2)	RCT	E 145215-00-5
	RGT	G 1310-58-3 KOH
	PRO	F 135345-84-5
RX(4)	RCT	F 135345-84-5, I 541-41-3
	RGT	J 26628-22-8 NaN3
	PRO	K 135345-85-6
RX(5)	RCT	K 135345-85-6
	RGT	M 7664-41-7 NH3
	PRO	L 135345-89-0
RX(8)	RCT	R 99471-66-6, L 135345-89-0
	PRO	S 135345-90-3
RX(9)	RCT	S 135345-90-3
	RGT	M 7664-41-7 NH3
	PRO	T 135345-91-4
RX(10)	RCT	T 135345-91-4
	PRO	U 135345-83-4
	NTE	H2/PD
RX(11)	RCT	U 135345-83-4, V 108-24-7
	PRO	W 145215-09-4
RX(13)	RCT	W 145215-09-4
	RGT	AA 10377-51-2 LiI
	PRO	Z 145215-11-8
	NTE	(NH4)2[CE(NO3)6]
RX(15)	RCT	Z 145215-11-8
	RGT	AC 124-41-4 NaOMe
	PRO	AE 145215-14-1

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SOL 67-56-1 MeOH

RX(16) RCT AF 96-33-3, AE 145215-14-1  
 RGT AH 603-35-0 PPh3  
 PRO AG 145215-18-5  
 CAT 3375-31-3 Pd(OAc)2

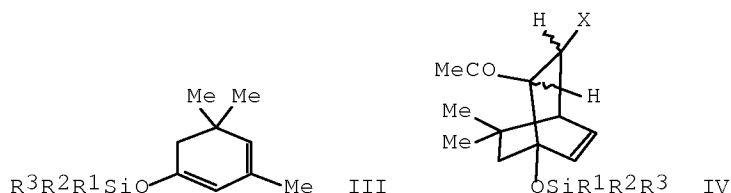
RX(17) RCT AG 145215-18-5  
 RGT AK 1310-73-2 NaOH  
 PRO AJ 145215-19-6

RX(18) RCT AJ 145215-19-6  
 RGT AM 128-08-5 Bromosuccinimide  
 PRO AL 145215-20-9

L46 ANSWER 15 OF 24 CASREACT COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 117:48950 CASREACT Full-text  
 TITLE: Preparation of 3-oxo- $\alpha$ -ionone  
 INVENTOR(S): Ito, Nobuhiko; Kinoshita, Kimio; Eto, Takeaki  
 PATENT ASSIGNEE(S): Soda Aromatic Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04041455	A	19920212	JP 1990-146361	19900606
JP 2929218	B2	19990803		
PRIORITY APPLN. INFO.:			JP 1990-146361	19900606
OTHER SOURCE(S):		MARPAT 117:48950		

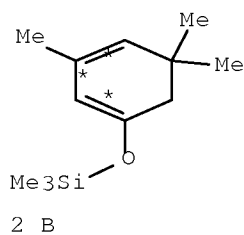
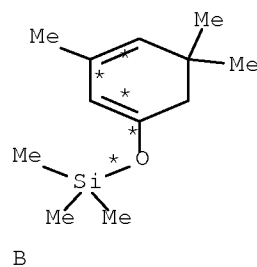
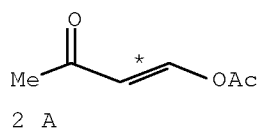
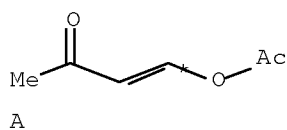
GI



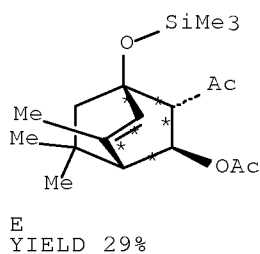
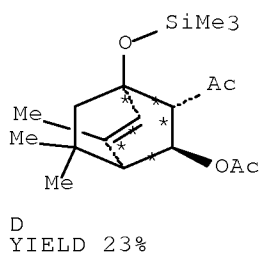
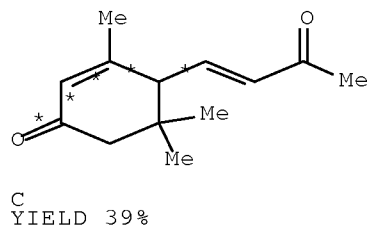
AB The title compound (I) is prepared by treating XCH:CHCOMe (II; X = alkoxy, acyloxy) with cyclohexadienes III (R1-R3 = C1-5 aliphatic hydrocarbyl) in the presence of Lewis acids, then optional treating with acids. Bicyclooctenes IV, useful as intermediates for I, are also prepared. A solution of AlCl3 in CH2Cl2 was treated dropwise with a solution of II (X = AcO) in CH2Cl2 at -3° over 2 min, then with a solution of III (R1 = R2 = R3 = Me) in CH2Cl2 over 13 min, and stirred at -3° for 2 h to give a mixture containing I 39.3, 7-endo-8-exo-IV 23.6, 7-exo-8-endo-IV 29.2%.

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RX(1) OF 6      3 A + 3 B ==> C + D +  
E...



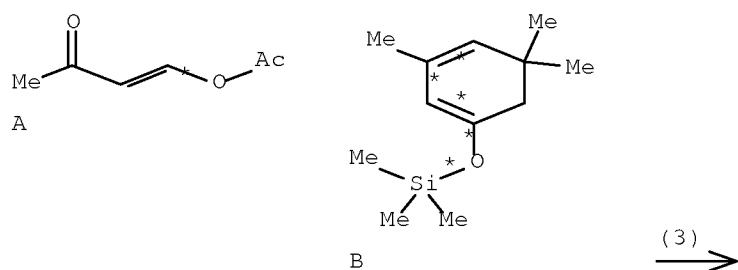
(1) →



RX(1)      RCT    A 13945-19-2, B 80699-65-6  
             PRO    C 20194-68-7, D 141915-26-6, E 141979-75-1  
             CAT    7446-70-0 AlCl3  
             SOL    75-09-2 CH2Cl2

RX(3) OF 6      A + B ==> C

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RX(3) RCT A 13945-19-2, B 80699-65-6

STAGE(1)

CAT 7446-70-0 AlCl<sub>3</sub>

SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

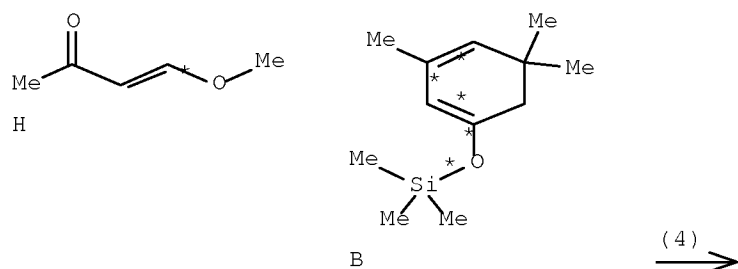
STAGE(2)

RGT L 7664-93-9 H<sub>2</sub>SO<sub>4</sub>

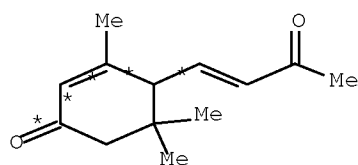
SOL 7732-18-5 Water, 67-56-1 MeOH

PRO C 20194-68-7

RX(4) OF 6 H + B ==> C



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C  
YIELD 67%

RX(4) RCT H 4652-27-1, B 80699-65-6

STAGE(1)

CAT 7446-70-0 AlCl3

SOL 75-09-2 CH2Cl2

STAGE(2)

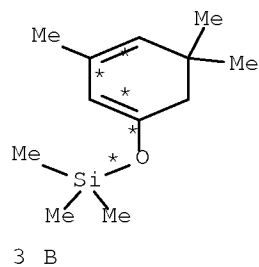
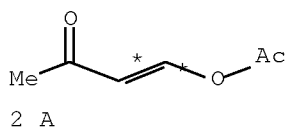
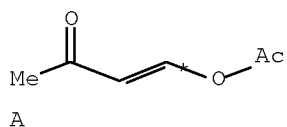
RGT L 7664-93-9 H2SO4

SOL 7732-18-5 Water, 67-56-1 MeOH

PRO C 20194-68-7

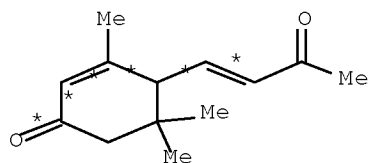
RX(6) OF 6 COMPOSED OF RX(1), RX(5)

RX(6) 3 A + 3 B ==> 2 C

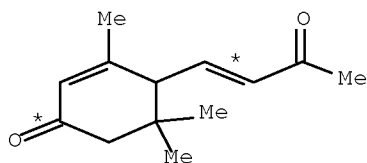


2  
STEPS  
→

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C  
YIELD 96%



C  
YIELD 96%

RX(1) RCT A 13945-19-2, B 80699-65-6  
PRO C 20194-68-7, D 141915-26-6, E 141979-75-1  
CAT 7446-70-0 AlCl3  
SOL 75-09-2 CH2Cl2

RX(5) RCT D 141915-26-6, E 141979-75-1  
RGT L 7664-93-9 H2SO4  
PRO C 20194-68-7  
SOL 7732-18-5 Water, 67-56-1 MeOH

L46 ANSWER 16 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 111:233390 CASREACT [Full-text](#)

TITLE: A colorimetric method for the estimation of  
2-deoxy-3-C-methyl-branched sugars

AUTHOR(S): Lo, Stanley F.; Yu, Yuan; Yang, Ding Yah; Liu, Hung  
Wen

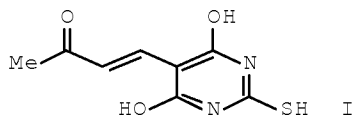
CORPORATE SOURCE: Dep. Chem., Univ. Minnesota, Minneapolis, MN, 55455,  
USA

SOURCE: Carbohydrate Research (1989), 189, 368-73  
CODEN: CRBRAT; ISSN: 0008-6215

DOCUMENT TYPE: Journal

LANGUAGE: English

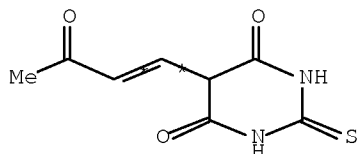
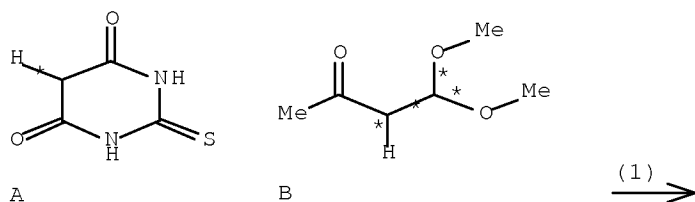
GI



AB The title method is based on the oxidation of the 2-deoxy-3-C-methyl-branched  
sugars, e.g., L-mycarose, with NaIO4 and condensation of the MeCOCH2CHO formed  
with 2-thiobarbituric acid to give pyrimidine derivative I, which can be  
quantified spectrophotometrically at 372 nm.

RX(1) OF 1 A + B ==> C

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C  
YIELD 86%

RX(1) RCT A 504-17-6, B 5436-21-5  
RGT D 7647-01-0 HCl  
PRO C 123765-14-0

L46 ANSWER 17 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 111:58252 CASREACT [Full-text](#)

TITLE: Synthesis and antiviral activity of the enantiomeric forms of carba-5-iodo-2'-deoxyuridine and carba-(E)-5-(2-bromovinyl)-2'-deoxyuridine

AUTHOR(S): Balzarini, Jan; Baumgartner, Harald; Bodenteich, Michael; De Clercq, Erik; Griengl, Herfried

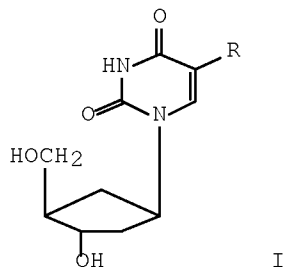
CORPORATE SOURCE: Inst. Org. Chem., Graz Univ. Technol., Graz, A-8010, Austria

SOURCE: Journal of Medicinal Chemistry (1989), 32(8), 1861-5  
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

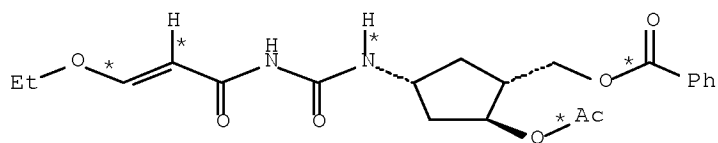




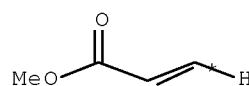
AB Both enantiomers of the carbocyclic analogs of 5-iodo-2'-deoxyuridine [(+)-I and (-)-I; R = iodo] and of (E)-5-(2-bromovinyl)-2'-deoxyuridine [(+)-I and (-)-I; R = (E)-CH:CHBr] were synthesized by using (+)- or (-)-endo-norborn-5-en-2-yl acetate or butyrate, resp., as starting materials. Against herpes simplex virus type 1, (+)-I (R = (E)-CH:CHBr) [(+)-C-BVDU] was only slightly less active than BVDU itself, whereas (-)-I [R = (E)-CH:CHBr] [(-)-C-BVDU] proved to be 10-400-fold less effective, depending on the strain investigated. Against HSV-2 both (+)- and (-)-C-BVDU as well as (+)- and (-)-C-IDU showed minor activity. All carbocyclic analogs were inactive against TK- HSV-1 strains, pointing to the prerequisite of phosphorylation (activation) by the viral thymidine kinase.

RX(100) OF 267 COMPOSED OF RX(21), RX(23), RX(25)

RX(100) AW + BF ==> BG

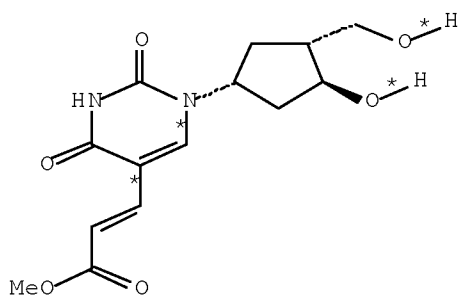


AW



BF

3  
STEPS  
→



BG  
YIELD 72%

RX(21) RCT AW 120905-35-3

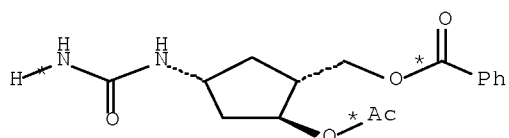
10/569486

RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

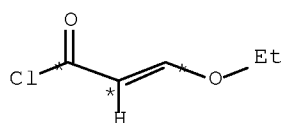
RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

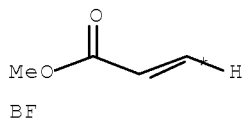
RX(101) OF 267 COMPOSED OF RX(19), RX(21), RX(23), RX(25)  
RX(101) AQ + AV + BF ==> BG



AQ

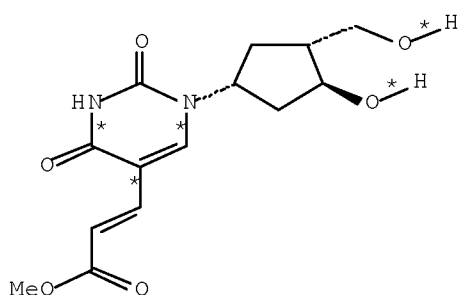


AV



BF

4  
STEPS  
→



BG  
YIELD 72%

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine

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PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

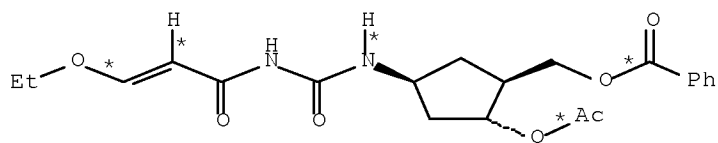
RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

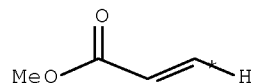
RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(102) OF 267 COMPOSED OF RX(22), RX(24), RX(26)

RX(102) AX + BF ==> BJ

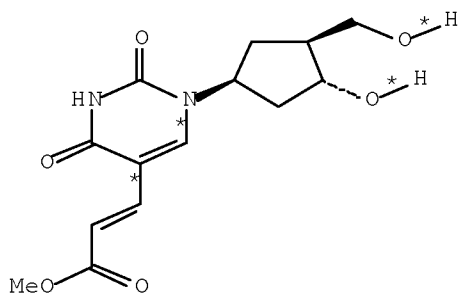


AX



BF

3  
STEPS  
→



BJ  
YIELD 72%

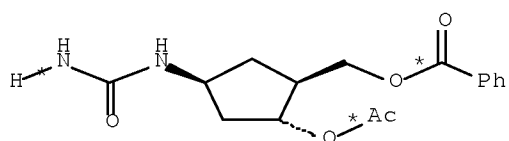
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RX(22) RCT AX 120963-42-0  
RGT AS 7664-41-7 NH3  
PRO AZ 120963-44-2  
SOL 7732-18-5 Water

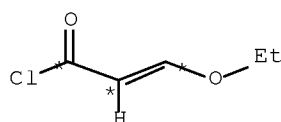
RX(24) RCT AZ 120963-44-2  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BE 120963-45-3  
SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BJ 120963-47-5  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

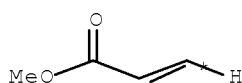
RX(103) OF 267 COMPOSED OF RX(20), RX(22), RX(24), RX(26)  
RX(103) AU + AV + BF ==> BJ



AU

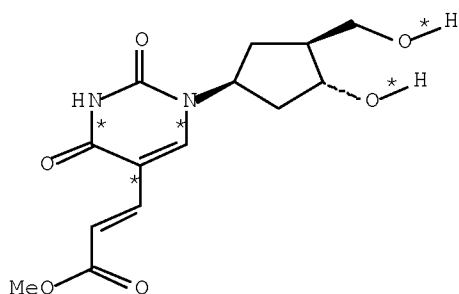


AV



BF

4  
STEPS  
→



BJ  
YIELD 72%

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RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH2Cl2

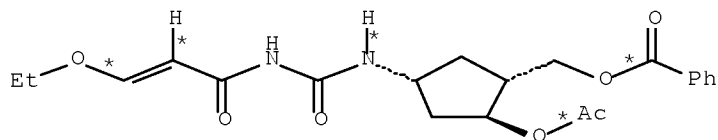
RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

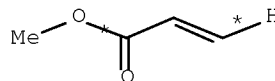
RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(105) OF 267 COMPOSED OF RX(21), RX(23), RX(25), RX(27)

RX(105) AW + BF ==> BK

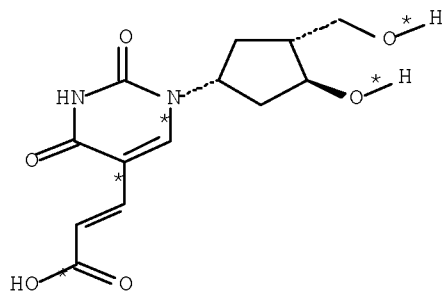


AW



BF

4  
 STEPS  
 →



BK

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RX(21) RCT AW 120905-35-3  
 RGT AS 7664-41-7 NH3  
 PRO AY 120963-43-1  
 SOL 7732-18-5 Water

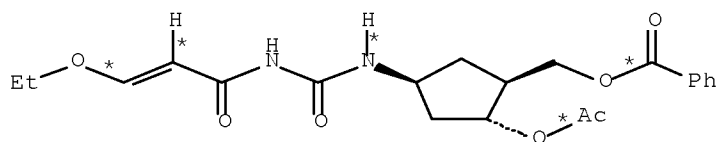
RX(23) RCT AY 120963-43-1  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BA 114179-59-8  
 SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BG 120963-46-4  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

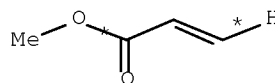
RX(27) RCT BG 120963-46-4  
 RGT BL 1310-58-3 KOH  
 PRO BK 120963-48-6

RX(107) OF 267 COMPOSED OF RX(22), RX(24), RX(26), RX(28)

RX(107) AX + BF ==> BM

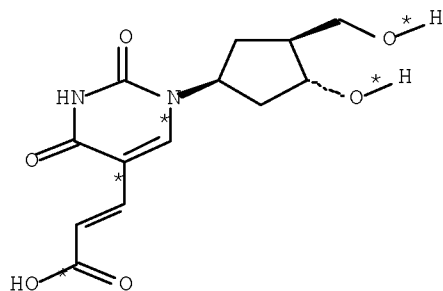


AX



BF

4  
 STEPS  
 →



BM

10/569486

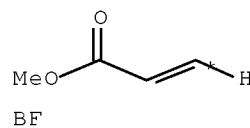
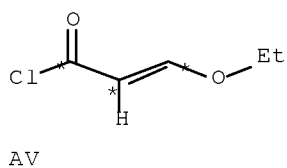
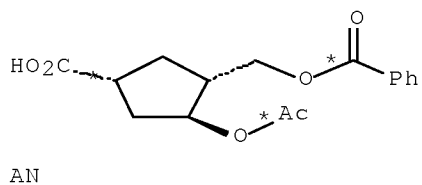
RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

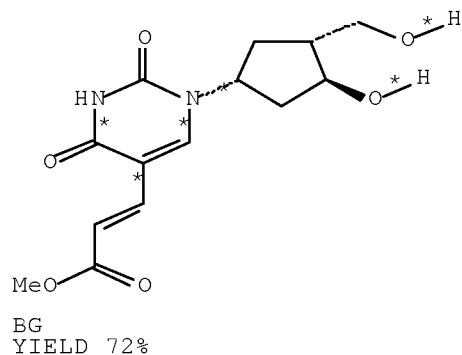
RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

RX(172) OF 267 COMPOSED OF RX(17), RX(19), RX(21), RX(23), RX(25)  
 RX(172) AN + AV + BF ==> EG



5  
 STEPS  
 →



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RX(17) RCT AN 120905-33-1

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3

SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7

RGT V 110-86-1 Pyridine

PRO AW 120905-35-3

SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3

RGT AS 7664-41-7 NH3

PRO AY 120963-43-1

SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1

RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3

PRO BA 114179-59-8

SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3

RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N

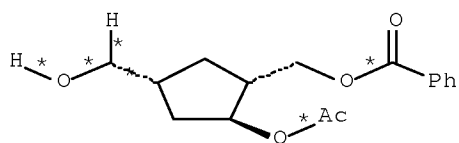
PRO BG 120963-46-4

CAT 3375-31-3 Pd(OAc)2

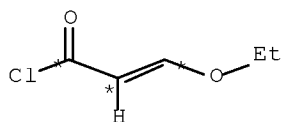
SOL 123-91-1 Dioxane

RX(173) OF 267 COMPOSED OF RX(15), RX(17), RX(19), RX(21), RX(23), RX(25)

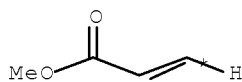
RX(173) AI + AV + BF ==> BG



AI



AV

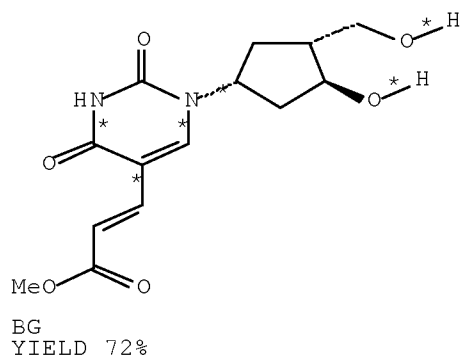


BF

6  
STEPS  
→



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```
RX(15)    RCT  AI 120905-32-0
          RGT  AO 20039-37-6 PDC
          PRO  AN 120905-33-1
          SOL  68-12-2 DMF

RX(17)    RCT  AN 120905-33-1

          STAGE(1)
            RGT  AR 26386-88-9 (PhO)2P(O)N3
            SOL  71-43-2 Benzene

          STAGE(2)
            RGT  AS 7664-41-7 NH3

          PRO  AQ 120905-34-2

RX(19)    RCT  AQ 120905-34-2, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AW 120905-35-3
          SOL  75-09-2 CH2Cl2

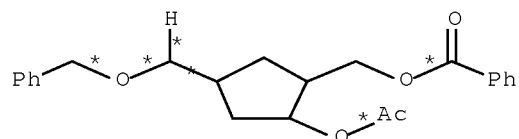
RX(21)    RCT  AW 120905-35-3
          RGT  AS 7664-41-7 NH3
          PRO  AY 120963-43-1
          SOL  7732-18-5 Water

RX(23)    RCT  AY 120963-43-1
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BA 114179-59-8
          SOL  123-91-1 Dioxane

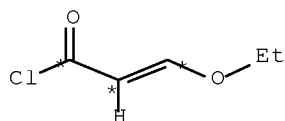
RX(25)    RCT  BA 114179-59-8, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BG 120963-46-4
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane
```

```
RX(174) OF 267 COMPOSED OF RX(13), RX(15), RX(17), RX(19), RX(21), RX(23),
          RX(25)
RX(174)  AC  +  AV  +  BF  ==>  EG
```

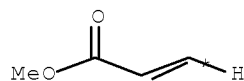
10/569486



AC

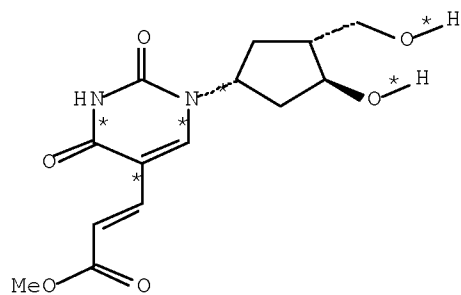


AV



BF

7  
STEPS  
→



BG  
YIELD 72%

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H2  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

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PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AW 120905-35-3  
 SOL 75-09-2 CH2Cl2

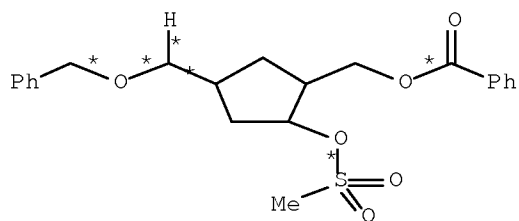
RX(21) RCT AW 120905-35-3  
 RGT AS 7664-41-7 NH3  
 PRO AY 120963-43-1  
 SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BA 114179-59-8  
 SOL 123-91-1 Dioxane

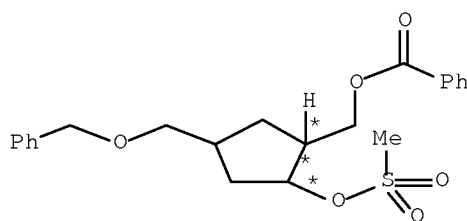
RX(25) RCT BA 114179-59-8, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BG 120963-46-4  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(175) OF 267 COMPOSED OF RX(11), RX(13), RX(15), RX(17), RX(19), RX(21),  
 RX(23), RX(25)

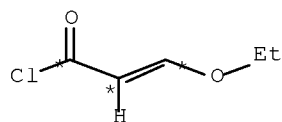
RX(175) 2 Z + AV + BF ==> BG



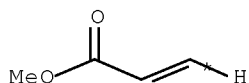
Z



Z



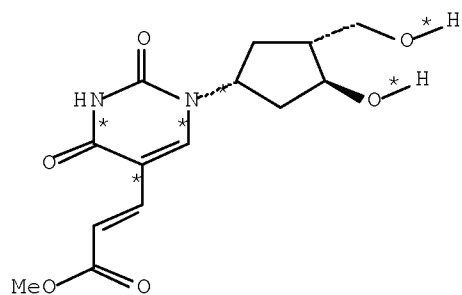
AV



BF

8  
 STEPS  
 →

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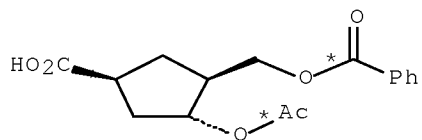
BG  
YIELD 72%

RX(11)	RCT	Z 116142-70-2
	RGT	AE 3396-11-0 Cs(OAc) <sub>2</sub>
	PRO	AC 120905-29-5, AD 120905-30-8
	SOL	67-68-5 DMSO
RX(13)	RCT	AC 120905-29-5
	RGT	AJ 1333-74-0 H <sub>2</sub>
	PRO	AI 120905-32-0
	CAT	7440-05-3 Pd
	SOL	64-17-5 EtOH
RX(15)	RCT	AI 120905-32-0
	RGT	AO 20039-37-6 PDC
	PRO	AN 120905-33-1
	SOL	68-12-2 DMF
RX(17)	RCT	AN 120905-33-1
	STAGE(1)	
	RGT	AR 26386-88-9 (PhO) <sub>2</sub> P(O)N <sub>3</sub>
	SOL	71-43-2 Benzene
	STAGE(2)	
	RGT	AS 7664-41-7 NH <sub>3</sub>
	PRO	AQ 120905-34-2
RX(19)	RCT	AQ 120905-34-2, AV 6191-99-7
	RGT	V 110-86-1 Pyridine
	PRO	AW 120905-35-3
	SOL	75-09-2 CH <sub>2</sub> Cl <sub>2</sub>
RX(21)	RCT	AW 120905-35-3
	RGT	AS 7664-41-7 NH <sub>3</sub>
	PRO	AY 120963-43-1
	SOL	7732-18-5 Water
RX(23)	RCT	AY 120963-43-1
	RGT	BB 7553-56-2 I <sub>2</sub> , BC 7697-37-2 HNO <sub>3</sub>
	PRO	BA 114179-59-8
	SOL	123-91-1 Dioxane

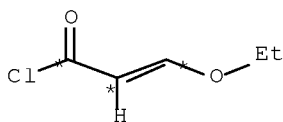
10/569486

RX(25) RCT BA 114179-59-8, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BG 120963-46-4  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

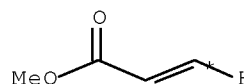
RX(176) OF 267 COMPOSED OF RX(18), RX(20), RX(22), RX(24), RX(26)  
 RX(176) AP + AV + BF ==> BJ



AP

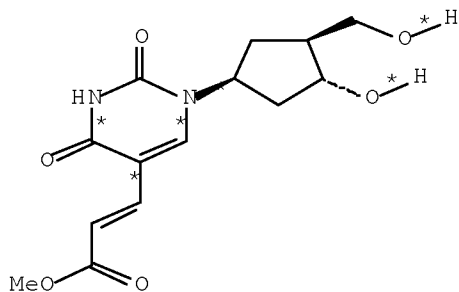


AV



BF

5  
 STEPS  
 →



BJ  
 YIELD 72%

RX(18) RCT AP 120963-40-8  
 STAGE(1)  
 RGT AR 26386-88-9 (PhO)2P(O)N3  
 SOL 71-43-2 Benzene

STAGE(2)  
 RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7

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RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

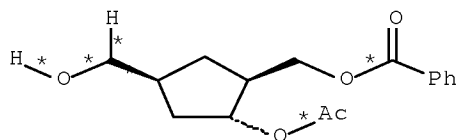
RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH<sub>3</sub>  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I<sub>2</sub>, BC 7697-37-2 HNO<sub>3</sub>  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

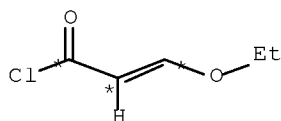
RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh<sub>3</sub>, AA 121-44-8 Et<sub>3</sub>N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)<sub>2</sub>  
 SOL 123-91-1 Dioxane

RX(177) OF 267 COMPOSED OF RX(16), RX(18), RX(20), RX(22), RX(24), RX(26)

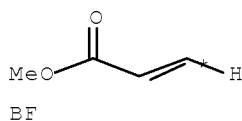
RX(177) AM + AV + BF ==> BJ



AM

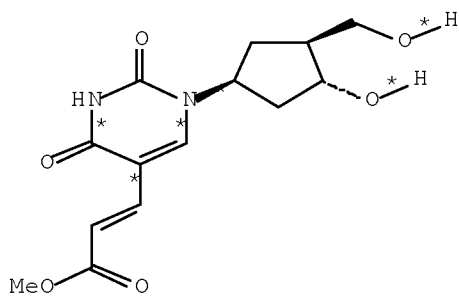


AV



BF

6  
 STEPS  
 →



BJ  
 YIELD 72%

RX(16)     RCT   AM 120963-39-5  
              RGT   AO 20039-37-6 PDC  
              PRO   AP 120963-40-8  
              SOL   68-12-2 DMF

RX(18)     RCT   AP 120963-40-8

             STAGE(1)  
                  RGT   AR 26386-88-9 (PhO)2P(O)N3  
                  SOL   71-43-2 Benzene

             STAGE(2)  
                  RGT   AS 7664-41-7 NH3

             PRO   AU 120963-41-9

RX(20)     RCT   AU 120963-41-9, AV 6191-99-7  
              RGT   V 110-86-1 Pyridine  
              PRO   AX 120963-42-0  
              SOL   75-09-2 CH2Cl2

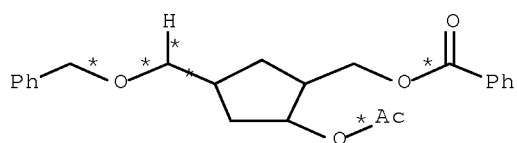
RX(22)     RCT   AX 120963-42-0  
              RGT   AS 7664-41-7 NH3  
              PRO   AZ 120963-44-2  
              SOL   7732-18-5 Water

RX(24)     RCT   AZ 120963-44-2  
              RGT   BB 7553-56-2 I2, BC 7697-37-2 HNO3  
              PRO   BE 120963-45-3  
              SOL   123-91-1 Dioxane

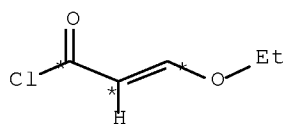
RX(26)     RCT   BE 120963-45-3, BF 96-33-3  
              RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N  
              PRO   BJ 120963-47-5  
              CAT   3375-31-3 Pd(OAc)2  
              SOL   123-91-1 Dioxane

RX(178) OF 267 COMPOSED OF RX(14), RX(16), RX(18), RX(20), RX(22), RX(24),  
 RX(26)

RX(178)     AG + AV + BF ==> EJ

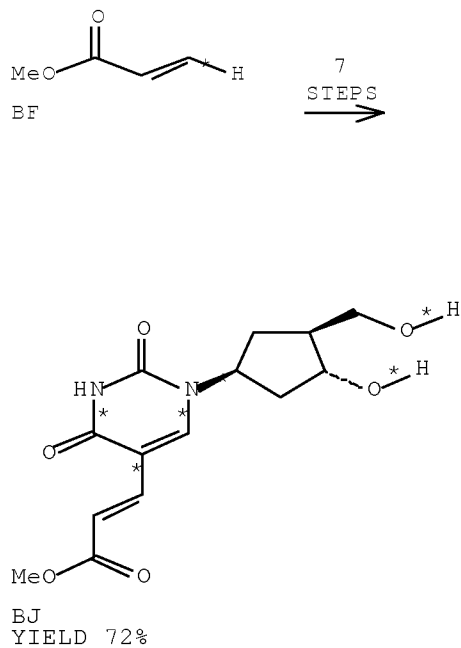


AG



AV

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RX(14)	RCT	AG	120963-38-4
	RGT	AJ	1333-74-0 H2
	PRO	AM	120963-39-5
	CAT	7440-05-3	Pd
	SOL	64-17-5	EtOH
RX(16)	RCT	AM	120963-39-5
	RGT	AO	20039-37-6 PDC
	PRO	AP	120963-40-8
	SOL	68-12-2	DMF
RX(18)	RCT	AP	120963-40-8
		STAGE(1)	
		RGT	AR 26386-88-9 (PhO)2P(O)N3
		SOL	71-43-2 Benzene
		STAGE(2)	
		RGT	AS 7664-41-7 NH3
	PRO	AU	120963-41-9
RX(20)	RCT	AU	120963-41-9, AV 6191-99-7
	RGT	V	110-86-1 Pyridine
	PRO	AX	120963-42-0
	SOL	75-09-2	CH2Cl2
RX(22)	RCT	AX	120963-42-0
	RGT	AS	7664-41-7 NH3
	PRO	AZ	120963-44-2
	SOL	7732-18-5	Water
RX(24)	RCT	AZ	120963-44-2



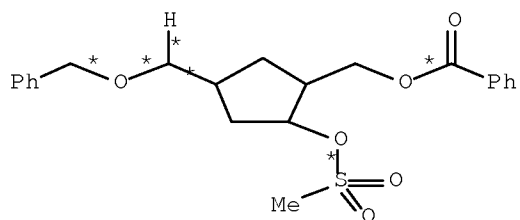
10/569486

RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

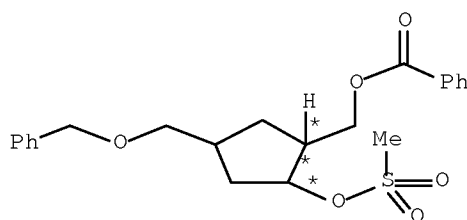
RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(179) OF 267 COMPOSED OF RX(12), RX(14), RX(16), RX(18), RX(20), RX(22),  
 RX(24), RX(26)

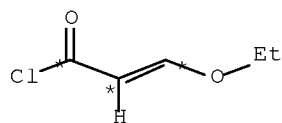
RX(179) 2 AB + AV + BF ==> BJ



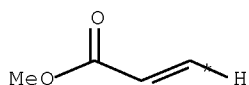
AB



AB

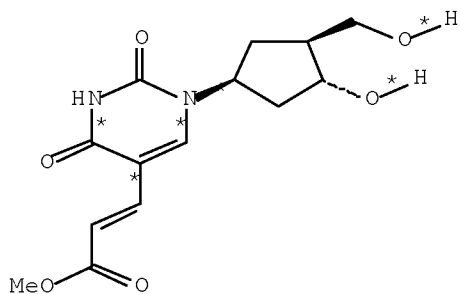


AV



BF

8  
 STEPS  
 →



BJ  
 YIELD 72%

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RX(12) RCT AB 120963-37-3  
 RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
 PRO AG 120963-38-4, AH 120905-31-9  
 SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
 RGT AJ 1333-74-0 H<sub>2</sub>  
 PRO AM 120963-39-5  
 CAT 7440-05-3 Pd  
 SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
 RGT AO 20039-37-6 PDC  
 PRO AP 120963-40-8  
 SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)

RGT AR 26386-88-9 (PhO)<sub>2</sub>P(O)N<sub>3</sub>  
 SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH<sub>3</sub>

PRO AU 120963-41-9

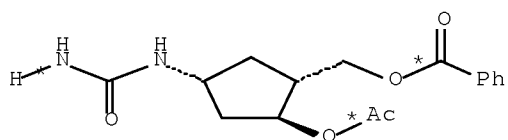
RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH<sub>3</sub>  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

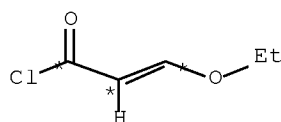
RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I<sub>2</sub>, BC 7697-37-2 HNO<sub>3</sub>  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh<sub>3</sub>, AA 121-44-8 Et<sub>3</sub>N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)<sub>2</sub>  
 SOL 123-91-1 Dioxane

RX(180) OF 267 COMPOSED OF RX(19), RX(21), RX(23), RX(25), RX(27)  
 RX(180) AQ + AV + BF ==> BK

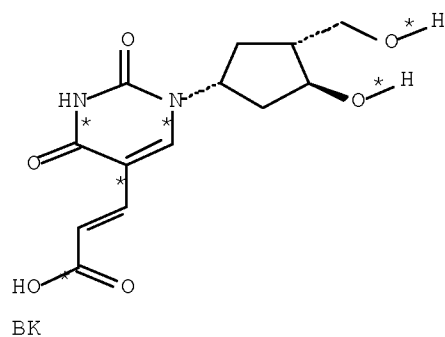
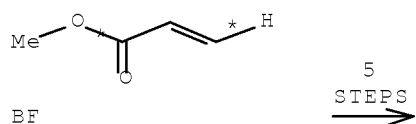


AQ



AV

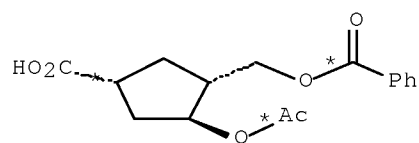
10/569486



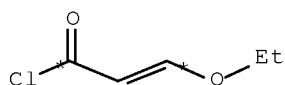
RX(19)	RCT	AQ 120905-34-2, AV 6191-99-7
	RGT	V 110-86-1 Pyridine
	PRO	AW 120905-35-3
	SOL	75-09-2 CH <sub>2</sub> Cl <sub>2</sub>
RX(21)	RCT	AW 120905-35-3
	RGT	AS 7664-41-7 NH <sub>3</sub>
	PRO	AY 120963-43-1
	SOL	7732-18-5 Water
RX(23)	RCT	AY 120963-43-1
	RGT	BB 7553-56-2 I <sub>2</sub> , BC 7697-37-2 HNO <sub>3</sub>
	PRO	BA 114179-59-8
	SOL	123-91-1 Dioxane
RX(25)	RCT	BA 114179-59-8, BF 96-33-3
	RGT	BH 603-35-0 PPh <sub>3</sub> , AA 121-44-8 Et <sub>3</sub> N
	PRO	BG 120963-46-4
	CAT	3375-31-3 Pd(OAc) <sub>2</sub>
	SOL	123-91-1 Dioxane
RX(27)	RCT	BG 120963-46-4
	RGT	BL 1310-58-3 KOH
	PRO	BK 120963-48-6

RX(181) OF 267 COMPOSED OF RX(17), RX(19), RX(21), RX(23), RX(25), RX(27)  
 RX(181) AN + AV + BF ==> BK

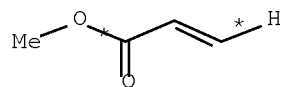
10/569486



AN

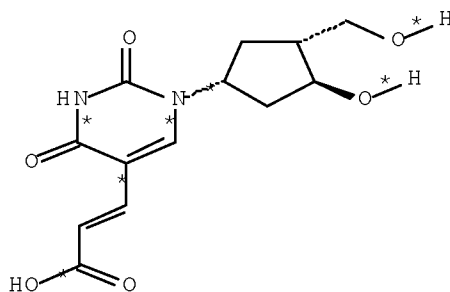


AV



BF

6  
STEPS  
→



BK

RX(17) RCT AN 120905-33-1

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3

SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7

RGT V 110-86-1 Pyridine

PRO AW 120905-35-3

SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3

RGT AS 7664-41-7 NH3

PRO AY 120963-43-1

SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1

RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3

PRO BA 114179-59-8

SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3

RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N

PRO BG 120963-46-4

CAT 3375-31-3 Pd(OAc)2

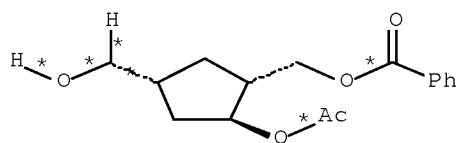
SOL 123-91-1 Dioxane

10/569486

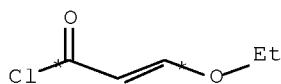
RX(27)      RCT    BG 120963-46-4  
              RGT    BL 1310-58-3 KOH  
              PRO    BK 120963-48-6

RX(182) OF 267 COMPOSED OF RX(15), RX(17), RX(19), RX(21), RX(23), RX(25),  
              RX(27)

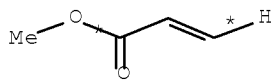
RX(182)    AI   +   AV   +   BF   ==>   BK



AI

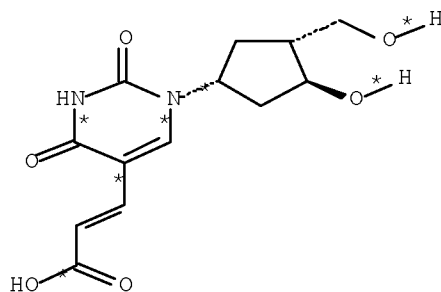


AV



BF

7  
STEPS  
→



BK

RX(15)      RCT    AI 120905-32-0  
              RGT    AO 20039-37-6 PDC  
              PRO    AN 120905-33-1  
              SOL    68-12-2 DMF

RX(17)      RCT    AN 120905-33-1

STAGE(1)

              RGT    AR 26386-88-9 (PhO)2P(O)N3

              SOL    71-43-2 Benzene

STAGE(2)

10/569486

RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

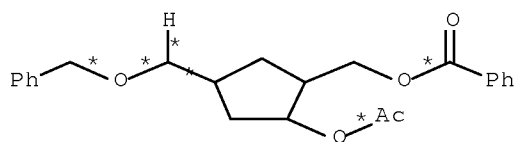
RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

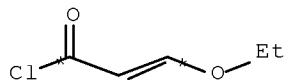
RX(27) RCT BG 120963-46-4  
RGT BL 1310-58-3 KOH  
PRO BK 120963-48-6

RX(183) OF 267 COMPOSED OF RX(13), RX(15), RX(17), RX(19), RX(21), RX(23),  
RX(25), RX(27)

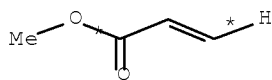
RX(183) AC + AV + BF ==> EK



AC



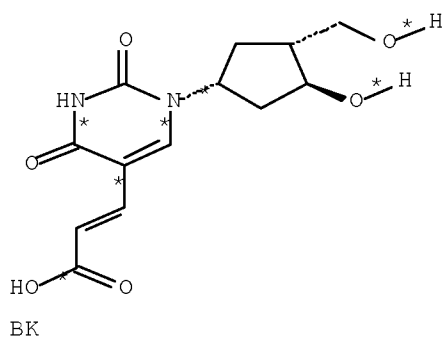
AV



BF

8  
STEPS  
→

10/569486

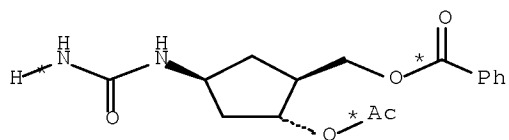


RX(13)	RCT	AC 120905-29-5
	RGT	AJ 1333-74-0 H2
	PRO	AI 120905-32-0
	CAT	7440-05-3 Pd
	SOL	64-17-5 EtOH
RX(15)	RCT	AI 120905-32-0
	RGT	AO 20039-37-6 PDC
	PRO	AN 120905-33-1
	SOL	68-12-2 DMF
RX(17)	RCT	AN 120905-33-1
	STAGE(1)	
	RGT	AR 26386-88-9 (PhO)2P(O)N3
	SOL	71-43-2 Benzene
	STAGE(2)	
	RGT	AS 7664-41-7 NH3
	PRO	AQ 120905-34-2
RX(19)	RCT	AQ 120905-34-2, AV 6191-99-7
	RGT	V 110-86-1 Pyridine
	PRO	AW 120905-35-3
	SOL	75-09-2 CH2Cl2
RX(21)	RCT	AW 120905-35-3
	RGT	AS 7664-41-7 NH3
	PRO	AY 120963-43-1
	SOL	7732-18-5 Water
RX(23)	RCT	AY 120963-43-1
	RGT	BB 7553-56-2 I2, BC 7697-37-2 HNO3
	PRO	BA 114179-59-8
	SOL	123-91-1 Dioxane
RX(25)	RCT	BA 114179-59-8, BF 96-33-3
	RGT	BH 603-35-0 PPh3, AA 121-44-8 Et3N
	PRO	BG 120963-46-4
	CAT	3375-31-3 Pd(OAc)2
	SOL	123-91-1 Dioxane

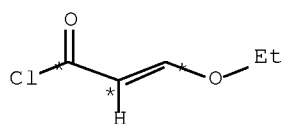
10/569486

RX(27) RCT BG 120963-46-4  
 RGT BL 1310-58-3 KOH  
 PRO BK 120963-48-6

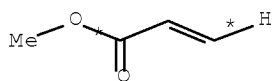
RX(184) OF 267 COMPOSED OF RX(20), RX(22), RX(24), RX(26), RX(28)  
 RX(184) AU + AV + BF ==> BM



AU

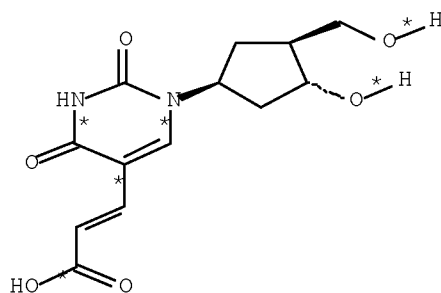


AV



BF

5  
 STEPS  
 →



BM

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

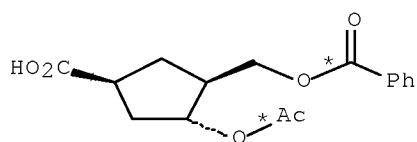


10/569486

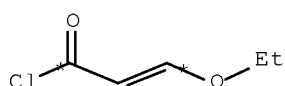
RX(26) RCT BE 120963-45-3, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BJ 120963-47-5  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
RGT BL 1310-58-3 KOH  
PRO BM 120963-49-7

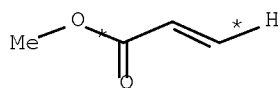
RX(185) OF 267 COMPOSED OF RX(18), RX(20), RX(22), RX(24), RX(26), RX(28)  
RX(185) AP + AV + BF ==> EM



AP

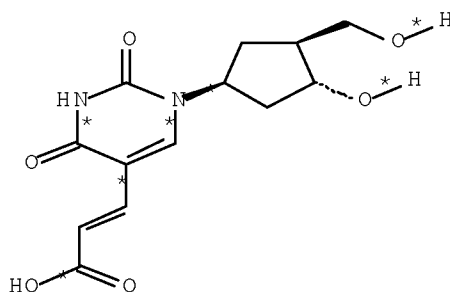


AV



BF

6  
STEPS  
→



BM

RX(18) RCT AP 120963-40-8

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AX 120963-42-0  
SOL 75-09-2 CH2Cl2

10/569486

RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

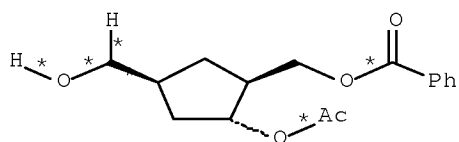
RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

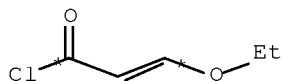
RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

RX(186) OF 267 COMPOSED OF RX(16), RX(18), RX(20), RX(22), RX(24), RX(26),  
 RX(28)

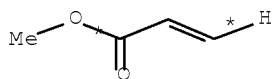
RX(186) AM + AV + BF ==> EM



AM

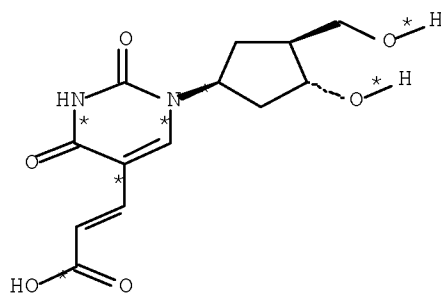


AV



BF

7  
 STEPS  
 →



EM

RX(16) RCT AM 120963-39-5  
 RGT AO 20039-37-6 PDC  
 PRO AP 120963-40-8  
 SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)  
 RGT AR 26386-88-9 (PhO)2P(O)N3  
 SOL 71-43-2 Benzene

STAGE(2)  
 RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

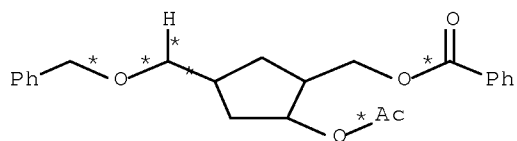
RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

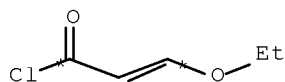
RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

RX(187) OF 267 COMPOSED OF RX(14), RX(16), RX(18), RX(20), RX(22), RX(24),  
 RX(26), RX(28)

RX(187) AG + AV + BF ==> BM

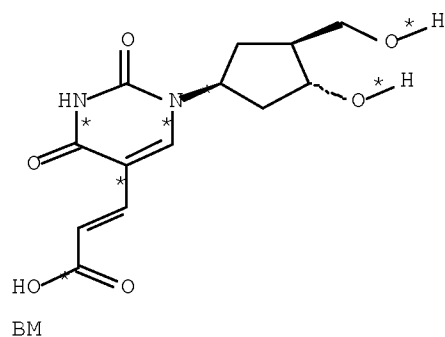
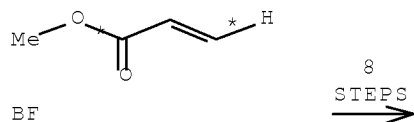


AG



AV

10/569486



RX(14)	RCT	AG 120963-38-4
	RGT	AJ 1333-74-0 H2
	PRO	AM 120963-39-5
	CAT	7440-05-3 Pd
	SOL	64-17-5 EtOH
RX(16)	RCT	AM 120963-39-5
	RGT	AO 20039-37-6 PDC
	PRO	AP 120963-40-8
	SOL	68-12-2 DMF
RX(18)	RCT	AP 120963-40-8
	STAGE(1)	
	RGT	AR 26386-88-9 (PhO)2P(O)N3
	SOL	71-43-2 Benzene
	STAGE(2)	
	RGT	AS 7664-41-7 NH3
	PRO	AU 120963-41-9
RX(20)	RCT	AU 120963-41-9, AV 6191-99-7
	RGT	V 110-86-1 Pyridine
	PRO	AX 120963-42-0
	SOL	75-09-2 CH2Cl2
RX(22)	RCT	AX 120963-42-0
	RGT	AS 7664-41-7 NH3
	PRO	AZ 120963-44-2
	SOL	7732-18-5 Water
RX(24)	RCT	AZ 120963-44-2

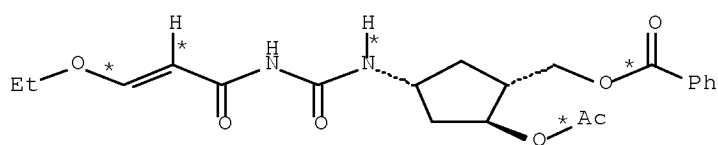
10/569486

RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

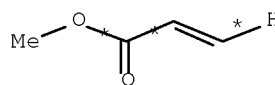
RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

RX(188) OF 267 COMPOSED OF RX(21), RX(23), RX(25), RX(27), RX(29)  
 RX(188) AW + BF ==> BN

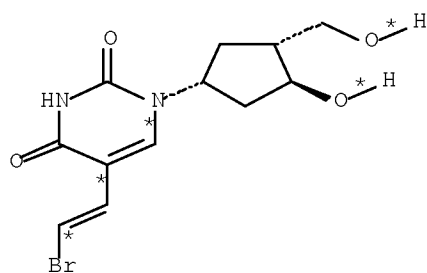


AW



BF

5  
 STEPS  
 →



BN

RX(21) RCT AW 120963-35-3  
 RGT AS 7664-41-7 NH3  
 PRO AY 120963-43-1  
 SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3

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PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

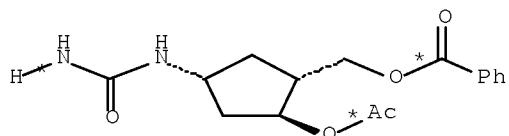
RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(27) RCT BG 120963-46-4  
RGT BL 1310-58-3 KOH  
PRO BK 120963-48-6

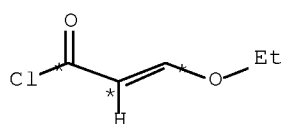
RX(29) RCT BK 120963-48-6  
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
PRO BN 95463-56-2  
SOL 68-12-2 DMF

RX(189) OF 267 COMPOSED OF RX(19), RX(21), RX(23), RX(25), RX(27), RX(29)

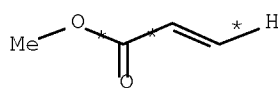
RX(189) AQ + AV + BF ==> BN



AQ

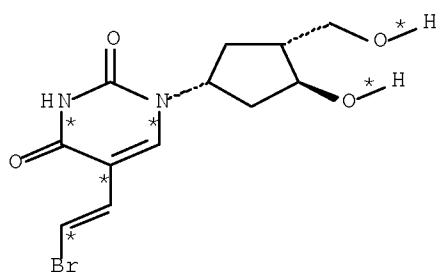


AV



BF

6  
STEPS  
→



BN

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

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RX(23) RCT AY 120963-43-1  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BA 114179-59-8  
 SOL 123-91-1 Dioxane

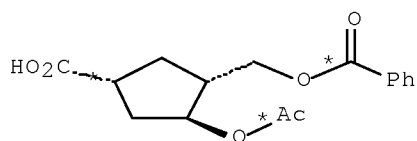
RX(25) RCT BA 114179-59-8, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BG 120963-46-4  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(27) RCT BG 120963-46-4  
 RGT BL 1310-58-3 KOH  
 PRO BK 120963-48-6

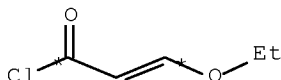
RX(29) RCT BK 120963-48-6  
 RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
 PRO BN 95463-56-2  
 SOL 68-12-2 DMF

RX(190) OF 267 COMPOSED OF RX(17), RX(19), RX(21), RX(23), RX(25), RX(27),  
 RX(29)

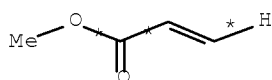
RX(190) AN + AV + BF ==> EN



AN

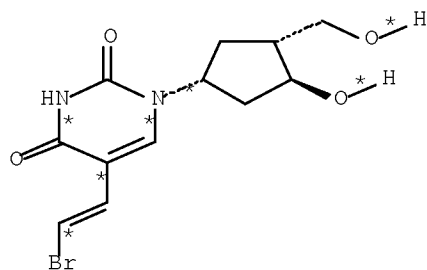


AV



BF

7  
 STEPS  
 →



BN

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RX(17) RCT AN 120905-33-1

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3

SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7

RGT V 110-86-1 Pyridine

PRO AW 120905-35-3

SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3

RGT AS 7664-41-7 NH3

PRO AY 120963-43-1

SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1

RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3

PRO BA 114179-59-8

SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3

RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N

PRO BG 120963-46-4

CAT 3375-31-3 Pd(OAc)2

SOL 123-91-1 Dioxane

RX(27) RCT BG 120963-46-4

RGT BL 1310-58-3 KOH

PRO BK 120963-48-6

RX(29) RCT BK 120963-48-6

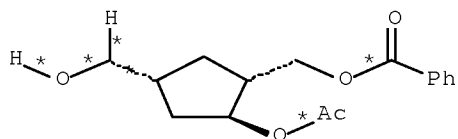
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide

PRO BN 95463-56-2

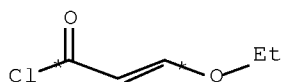
SOL 68-12-2 DMF

RX(191) OF 267 COMPOSED OF RX(15), RX(17), RX(19), RX(21), RX(23), RX(25),  
RX(27), RX(29)

RX(191) AI + AV + BF ==> BN



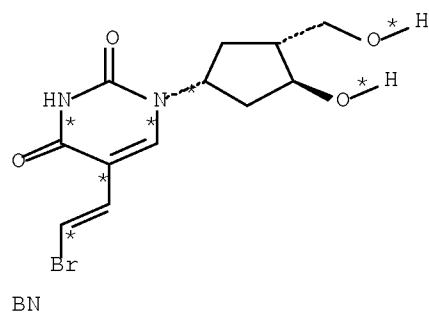
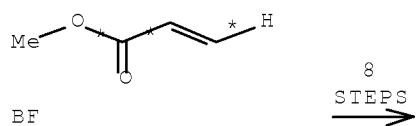
AI



AV



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RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)  
RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)  
RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2

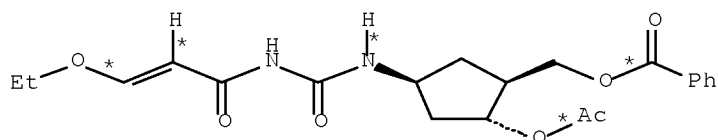
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SOL 123-91-1 Dioxane

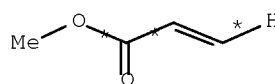
RX(27) RCT BG 120963-46-4  
RGT BL 1310-58-3 KOH  
PRO BK 120963-48-6

RX(29) RCT BK 120963-48-6  
RGT BO 298-14-6 KHCO<sub>3</sub>, BP 128-08-5 Bromosuccinimide  
PRO BN 95463-56-2  
SOL 68-12-2 DMF

RX(192) OF 267 COMPOSED OF RX(22), RX(24), RX(26), RX(28), RX(30)  
RX(192) AX + BF ==> BQ

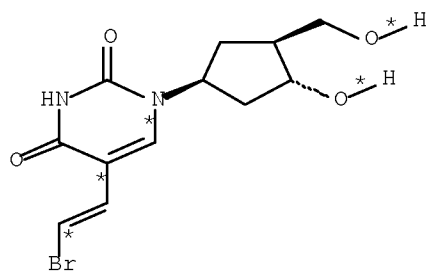


AX



BF

5  
STEPS  
→



BQ

RX(22) RCT AX 120963-42-0  
RGT AS 7664-41-7 NH<sub>3</sub>  
PRO AZ 120963-44-2  
SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
RGT BB 7553-56-2 I<sub>2</sub>, BC 7697-37-2 HNO<sub>3</sub>  
PRO BE 120963-45-3  
SOL 123-91-1 Dioxane

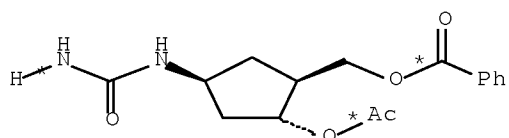
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RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

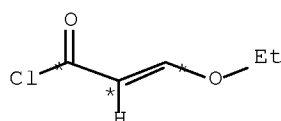
RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

RX(30) RCT BM 120963-49-7  
 RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
 PRO BQ 120963-50-0  
 SOL 68-12-2 DMF

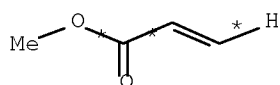
RX(193) OF 267 COMPOSED OF RX(20), RX(22), RX(24), RX(26), RX(28), RX(30)  
 RX(193) AU + AV + BF ==> BQ



AU

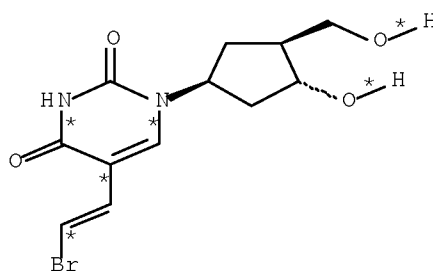


AV



BF

6  
 STEPS  
 →



BQ

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3

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SOL 123-91-1 Dioxane

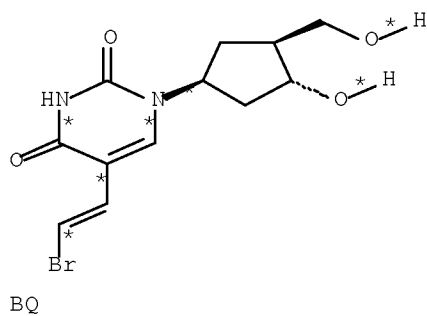
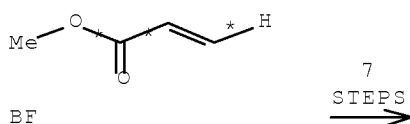
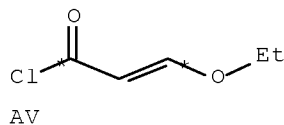
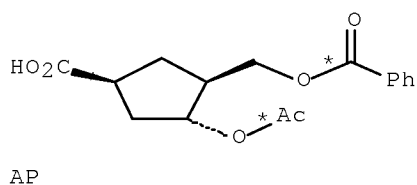
RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

RX(30) RCT BM 120963-49-7  
 RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
 PRO BQ 120963-50-0  
 SOL 68-12-2 DMF

RX(194) OF 267 COMPOSED OF RX(18), RX(20), RX(22), RX(24), RX(26), RX(28),  
 RX(30)

RX(194) AP + AV + BF ==> BQ



RX(18) RCT AP 120963-40-8

## STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3  
 SOL 71-43-2 Benzene

## STAGE(2)

RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

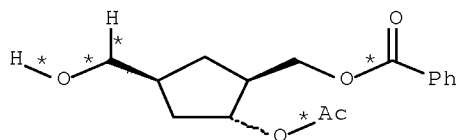
RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

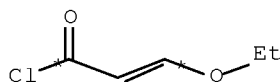
RX(30) RCT BM 120963-49-7  
 RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
 PRO BQ 120963-50-0  
 SOL 68-12-2 DMF

RX(195) OF 267 COMPOSED OF RX(16), RX(18), RX(20), RX(22), RX(24), RX(26),  
 RX(28), RX(30)

RX(195) AM + AV + BF ==> EQ

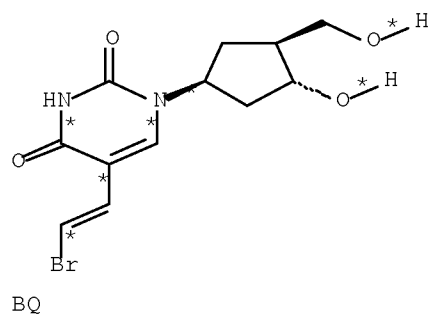
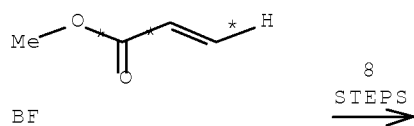


AM



AV

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RX(16)	RCT	AM 120963-39-5
	RGT	AO 20039-37-6 PDC
	PRO	AP 120963-40-8
	SOL	68-12-2 DMF
RX(18)	RCT	AP 120963-40-8
	STAGE(1)	
	RGT	AR 26386-88-9 (PhO)2P(O)N3
	SOL	71-43-2 Benzene
	STAGE(2)	
	RGT	AS 7664-41-7 NH3
	PRO	AU 120963-41-9
RX(20)	RCT	AU 120963-41-9, AV 6191-99-7
	RGT	V 110-86-1 Pyridine
	PRO	AX 120963-42-0
	SOL	75-09-2 CH2Cl2
RX(22)	RCT	AX 120963-42-0
	RGT	AS 7664-41-7 NH3
	PRO	AZ 120963-44-2
	SOL	7732-18-5 Water
RX(24)	RCT	AZ 120963-44-2
	RGT	BB 7553-56-2 I2, BC 7697-37-2 HNO3
	PRO	BE 120963-45-3
	SOL	123-91-1 Dioxane
RX(26)	RCT	BE 120963-45-3, BF 96-33-3
	RGT	BH 603-35-0 PPh3, AA 121-44-8 Et3N
	PRO	BJ 120963-47-5
	CAT	3375-31-3 Pd(OAc)2

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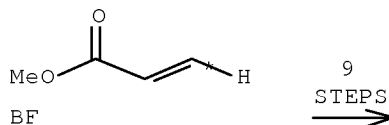
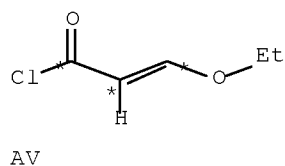
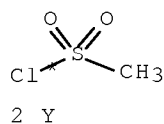
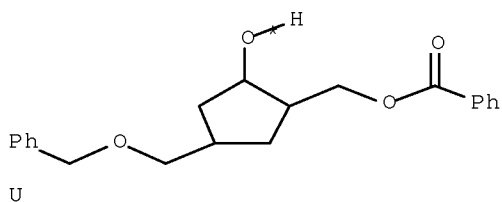
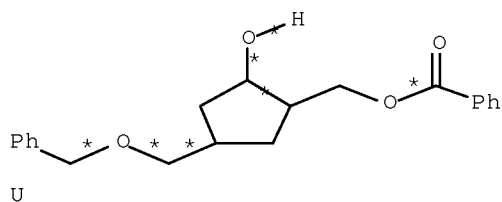
SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
RGT BL 1310-58-3 KOH  
PRO BM 120963-49-7

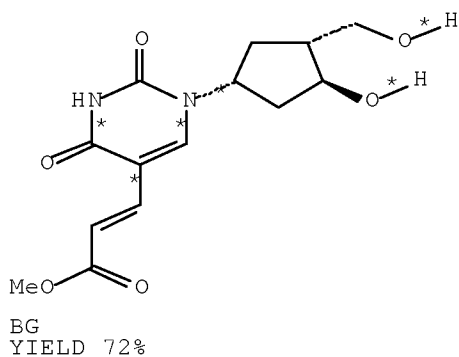
RX(30) RCT BM 120963-49-7  
RGT BO 298-14-6 KHCO<sub>3</sub>, BP 128-08-5 Bromosuccinimide  
PRO BQ 120963-50-0  
SOL 68-12-2 DMF

RX(226) OF 267 COMPOSED OF RX(9), RX(11), RX(13), RX(15), RX(17), RX(19),  
RX(21), RX(23), RX(25)

RX(226) 2 U + 2 Y + AV + BF ==> BG



9  
STEPS  
→



RX(9) RCT U 120236-99-9, Y 124-63-0

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RGT AA 121-44-8 Et3N  
PRO Z 116142-70-2  
SOL 75-09-2 CH2Cl2

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H2  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

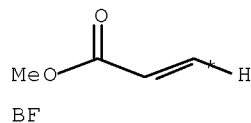
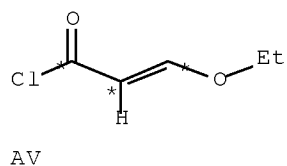
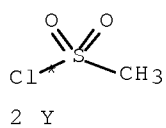
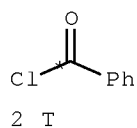
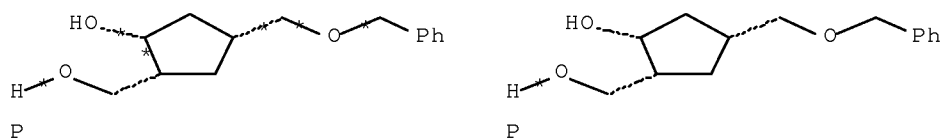
RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(227) OF 267 COMPOSED OF RX(7), RX(9), RX(11), RX(13), RX(15), RX(17),  
RX(19), RX(21), RX(23), RX(25)

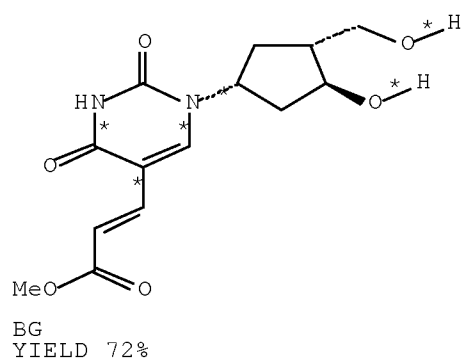
RX(227) 2 P + 2 T + 2 Y + AV + BF ==>  
EG



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10  
STEPS  
→



RX(7) RCT P 120236-98-8, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO U 120236-99-9  
SOL 75-09-2 CH2Cl2

RX(9) RCT U 120236-99-9, Y 124-63-0  
RGT AA 121-44-8 Et3N  
PRO Z 116142-70-2  
SOL 75-09-2 CH2Cl2

RX(11) RCT Z 116142-70-2

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RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H<sub>2</sub>  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)

RGT AR 26386-88-9 (PhO)<sub>2</sub>P(O)N<sub>3</sub>  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH<sub>3</sub>

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH<sub>3</sub>  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

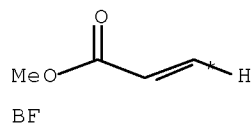
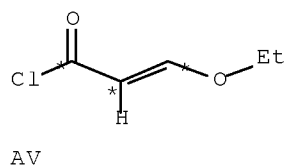
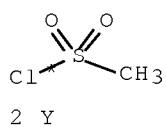
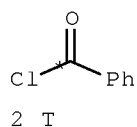
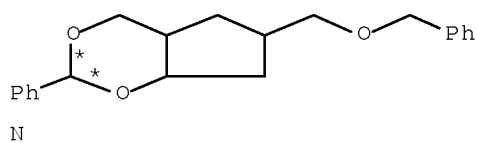
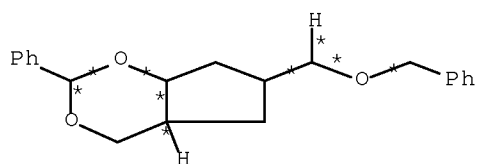
RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I<sub>2</sub>, BC 7697-37-2 HNO<sub>3</sub>  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh<sub>3</sub>, AA 121-44-8 Et<sub>3</sub>N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)<sub>2</sub>  
SOL 123-91-1 Dioxane

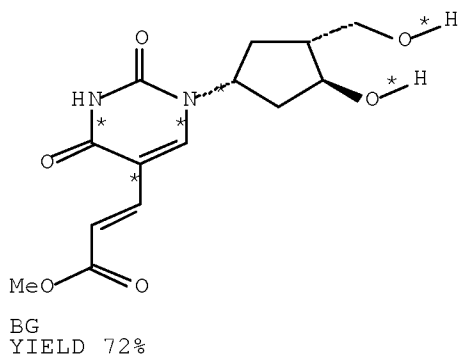
RX(228) OF 267 COMPOSED OF RX(5), RX(7), RX(9), RX(11), RX(13), RX(15), RX(17),  
RX(19), RX(21), RX(23), RX(25)

RX(228) 2 N + 2 T + 2 Y + AV + BF ==>  
EG

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11  
STEPS  
→



RX(5) RCT N 120905-28-4  
RGT Q 7664-93-9 H2SO4  
PRO P 120236-98-8  
SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO U 120236-99-9  
SOL 75-09-2 CH2Cl2

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RX(9) RCT U 120236-99-9, Y 124-63-0  
RGT AA 121-44-8 Et3N  
PRO Z 116142-70-2  
SOL 75-09-2 CH2Cl2

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H2  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)  
RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)  
RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

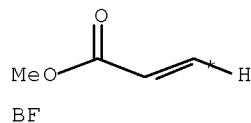
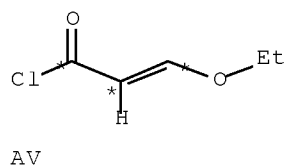
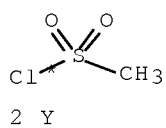
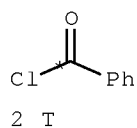
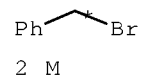
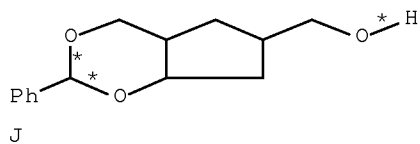
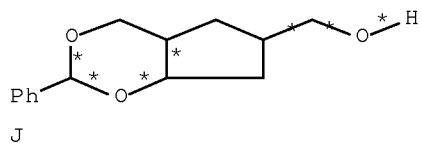
RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

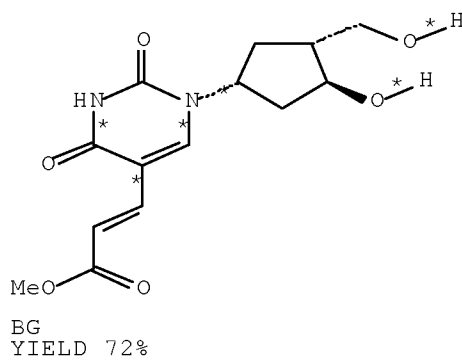
RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(229) OF 267 COMPOSED OF RX(4), RX(5), RX(7), RX(9), RX(11), RX(13), RX(15),  
RX(17), RX(19), RX(21), RX(23), RX(25)  
RX(229) 2 J + 2 M + 2 T + 2 Y + AV + BF ==>  
EG

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STEPS  
→



RX(4) RCT J 108275-94-1, M 100-39-0  
RGT O 7693-26-7 KH  
PRO N 120905-28-4  
SOL 109-99-9 THF

RX(5) RCT N 120905-28-4  
RGT Q 7664-93-9 H2SO4  
PRO P 120236-98-8  
SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO U 120236-99-9  
SOL 75-09-2 CH2Cl2

RX(9) RCT U 120236-99-9, Y 124-63-0  
RGT AA 121-44-8 Et3N  
PRO Z 116142-70-2

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```
SOL 75-09-2 CH2Cl2

RX(11)  RCT  Z 116142-70-2
        RGT  AE 3396-11-0 Cs(OAc)2
        PRO  AC 120905-29-5, AD 120905-30-8
        SOL  67-68-5 DMSO

RX(13)  RCT  AC 120905-29-5
        RGT  AJ 1333-74-0 H2
        PRO  AI 120905-32-0
        CAT  7440-05-3 Pd
        SOL  64-17-5 EtOH

RX(15)  RCT  AI 120905-32-0
        RGT  AO 20039-37-6 PDC
        PRO  AN 120905-33-1
        SOL  68-12-2 DMF

RX(17)  RCT  AN 120905-33-1

        STAGE(1)
            RGT  AR 26386-88-9 (PhO)2P(O)N3
            SOL  71-43-2 Benzene

        STAGE(2)
            RGT  AS 7664-41-7 NH3

        PRO  AQ 120905-34-2

RX(19)  RCT  AQ 120905-34-2, AV 6191-99-7
        RGT  V 110-86-1 Pyridine
        PRO  AW 120905-35-3
        SOL  75-09-2 CH2Cl2

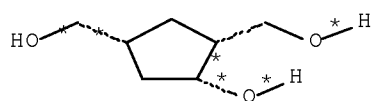
RX(21)  RCT  AW 120905-35-3
        RGT  AS 7664-41-7 NH3
        PRO  AY 120963-43-1
        SOL  7732-18-5 Water

RX(23)  RCT  AY 120963-43-1
        RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
        PRO  BA 114179-59-8
        SOL  123-91-1 Dioxane

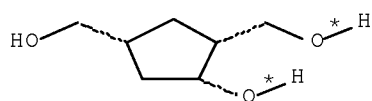
RX(25)  RCT  BA 114179-59-8, BF 96-33-3
        RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
        PRO  BG 120963-46-4
        CAT  3375-31-3 Pd(OAc)2
        SOL  123-91-1 Dioxane

RX(230) OF 267 COMPOSED OF RX(3), RX(4), RX(5), RX(7), RX(9), RX(11), RX(13),
        RX(15), RX(17), RX(19), RX(21), RX(23), RX(25)
RX(230) 2 B + I + 2 M + 2 T + 2 Y + AV + BF
        ==> EG
```

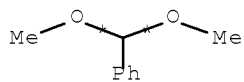
10/569486



B



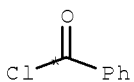
B



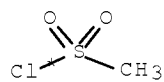
I



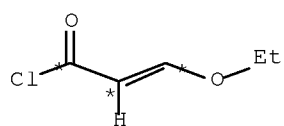
2 M



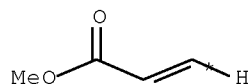
2 T



2 Y

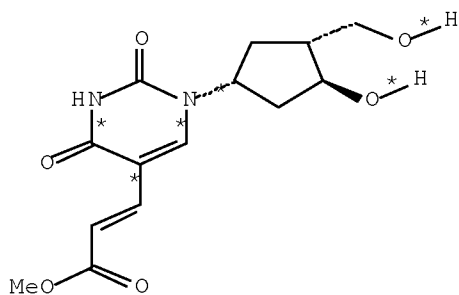


AV



BF

13  
STEPS  
→



BG  
YIELD 72%

RX(3) RCT B 114129-19-0, I 1125-88-8  
RGT K 16872-11-0 HBF<sub>4</sub>  
PRO J 108275-94-1  
SOL 68-12-2 DMF

RX(4) RCT J 108275-94-1, M 100-39-0  
RGT O 7693-26-7 KH  
PRO N 120905-28-4  
SOL 109-99-9 THF

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RX(5) RCT N 120905-28-4  
RGT Q 7664-93-9 H2SO4  
PRO P 120236-98-8  
SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO U 120236-99-9  
SOL 75-09-2 CH2Cl2

RX(9) RCT U 120236-99-9, Y 124-63-0  
RGT AA 121-44-8 Et3N  
PRO Z 116142-70-2  
SOL 75-09-2 CH2Cl2

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H2  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)  
RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)  
RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N

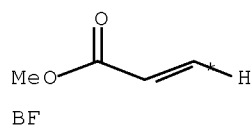
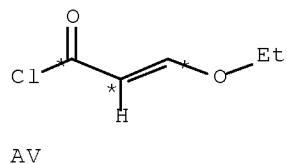
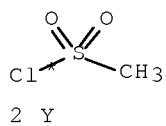
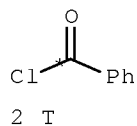
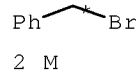
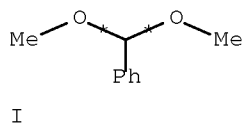
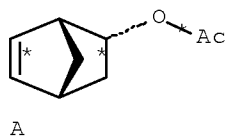
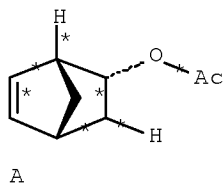


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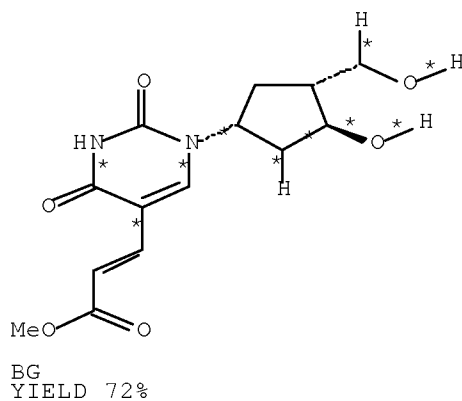
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)<sub>2</sub>  
SOL 123-91-1 Dioxane

RX(231) OF 267 COMPOSED OF RX(1), RX(3), RX(4), RX(5), RX(7), RX(9), RX(11),  
RX(13), RX(15), RX(17), RX(19), RX(21), RX(23), RX(25)

RX(231) 2 A + I + 2 M + 2 T + 2 Y + AV + BF  
====> BG



14  
STEPS  
→



RX(1) RCT A 112836-09-6

STAGE(1)  
RGT C 10028-15-6 Ozone  
SOL 67-56-1 MeOH

STAGE(2)

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RGT D 16853-85-3 LiAlH<sub>4</sub>  
SOL 109-99-9 THF

PRO B 114129-19-0

RX(3) RCT B 114129-19-0, I 1125-88-8  
RGT K 16872-11-0 HBF<sub>4</sub>  
PRO J 108275-94-1  
SOL 68-12-2 DMF

RX(4) RCT J 108275-94-1, M 100-39-0  
RGT O 7693-26-7 KH  
PRO N 120905-28-4  
SOL 109-99-9 THF

RX(5) RCT N 120905-28-4  
RGT Q 7664-93-9 H<sub>2</sub>SO<sub>4</sub>  
PRO P 120236-98-8  
SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO U 120236-99-9  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(9) RCT U 120236-99-9, Y 124-63-0  
RGT AA 121-44-8 Et<sub>3</sub>N  
PRO Z 116142-70-2  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H<sub>2</sub>  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)

RGT AR 26386-88-9 (PhO)<sub>2</sub>P(O)N<sub>3</sub>  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH<sub>3</sub>

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3

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SOL 75-09-2 CH2Cl2

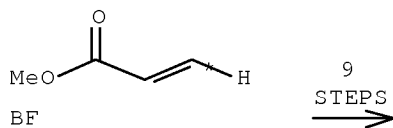
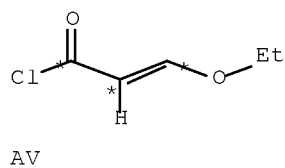
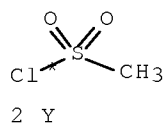
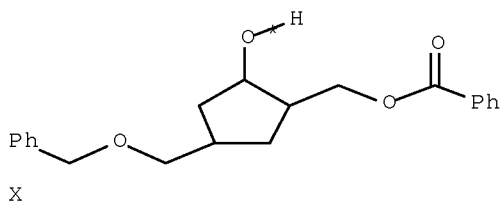
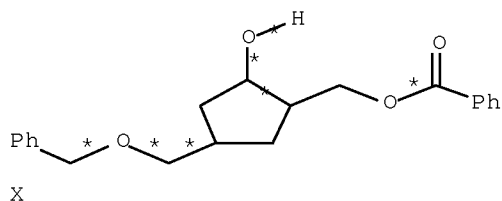
RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

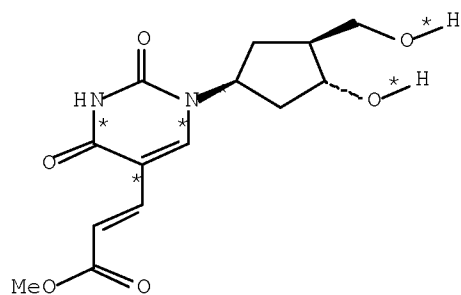
RX(232) OF 267 COMPOSED OF RX(10), RX(12), RX(14), RX(16), RX(18), RX(20),  
RX(22), RX(24), RX(26)

RX(232) 2 X + 2 Y + AV + BF ==> EJ



9  
STEPS  
→

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BJ  
YIELD 72%

```

RX(10)      RCT   X 120963-36-2, Y 124-63-0
             RGT   AA 121-44-8 Et3N
             PRO   AB 120963-37-3
             SOL   75-09-2 CH2Cl2

RX(12)      RCT   AB 120963-37-3
             RGT   AE 3396-11-0 Cs(OAc)2
             PRO   AG 120963-38-4, AH 120905-31-9
             SOL   67-68-5 DMSO

RX(14)      RCT   AG 120963-38-4
             RGT   AJ 1333-74-0 H2
             PRO   AM 120963-39-5
             CAT   7440-05-3 Pd
             SOL   64-17-5 EtOH

RX(16)      RCT   AM 120963-39-5
             RGT   AO 20039-37-6 PDC
             PRO   AP 120963-40-8
             SOL   68-12-2 DMF

RX(18)      RCT   AP 120963-40-8

             STAGE(1)
             RGT   AR 26386-88-9 (PhO)2P(O)N3
             SOL   71-43-2 Benzene

             STAGE(2)
             RGT   AS 7664-41-7 NH3

             PRO   AU 120963-41-9

RX(20)      RCT   AU 120963-41-9, AV 6191-99-7
             RGT   V 110-86-1 Pyridine
             PRO   AX 120963-42-0
             SOL   75-09-2 CH2Cl2

RX(22)      RCT   AX 120963-42-0
             RGT   AS 7664-41-7 NH3
             PRO   AZ 120963-44-2
             SOL   7732-18-5 Water

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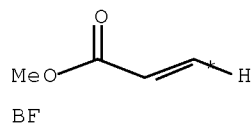
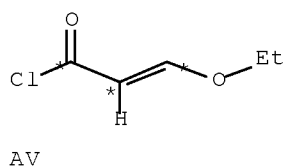
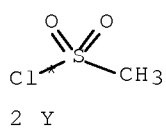
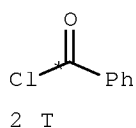
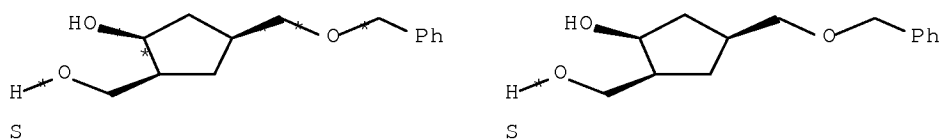
10/569486

RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

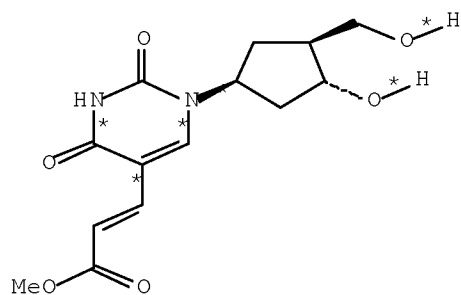
RX(233) OF 267 COMPOSED OF RX(8), RX(10), RX(12), RX(14), RX(16), RX(18),  
 RX(20), RX(22), RX(24), RX(26)

RX(233) 2 S + 2 T + 2 Y + AV + BF ==>  
 BJ



10  
 STEPS  
 →

10/569486



BJ  
YIELD 72%

RX(8) RCT S 120963-35-1, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO X 120963-36-2  
SOL 75-09-2 CH2Cl2

RX(10) RCT X 120963-36-2, Y 124-63-0  
RGT AA 121-44-8 Et3N  
PRO AB 120963-37-3  
SOL 75-09-2 CH2Cl2

RX(12) RCT AB 120963-37-3  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AG 120963-38-4, AH 120905-31-9  
SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
RGT AJ 1333-74-0 H2  
PRO AM 120963-39-5  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
RGT AO 20039-37-6 PDC  
PRO AP 120963-40-8  
SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AX 120963-42-0  
SOL 75-09-2 CH2Cl2

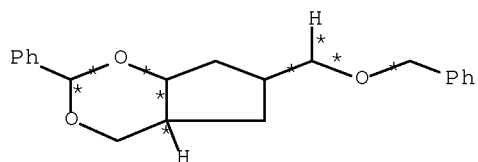
10/569486

RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

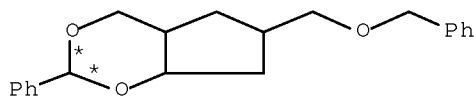
RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

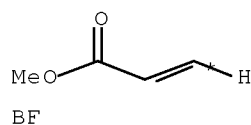
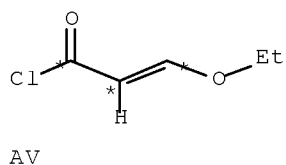
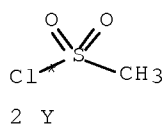
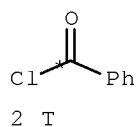
RX(234) OF 267 COMPOSED OF RX(6), RX(8), RX(10), RX(12), RX(14), RX(16),  
 RX(18), RX(20), RX(22), RX(24), RX(26)  
 RX(234) 2 N + 2 T + 2 Y + AV + BF ==>  
 BJ



N

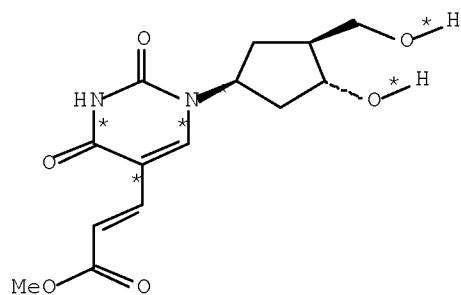


N



11  
 STEPS  
 →

10/569486



BJ  
YIELD 72%

RX(6) RCT N 120905-28-4  
RGT Q 7664-93-9 H2SO4  
PRO S 120963-35-1  
SOL 7732-18-5 Water

RX(8) RCT S 120963-35-1, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO X 120963-36-2  
SOL 75-09-2 CH2Cl2

RX(10) RCT X 120963-36-2, Y 124-63-0  
RGT AA 121-44-8 Et3N  
PRO AB 120963-37-3  
SOL 75-09-2 CH2Cl2

RX(12) RCT AB 120963-37-3  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AG 120963-38-4, AH 120905-31-9  
SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
RGT AJ 1333-74-0 H2  
PRO AM 120963-39-5  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
RGT AO 20039-37-6 PDC  
PRO AP 120963-40-8  
SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AU 120963-41-9



10/569486

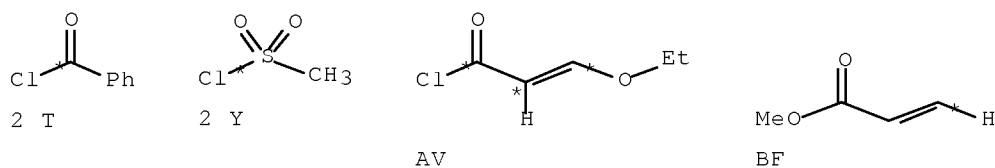
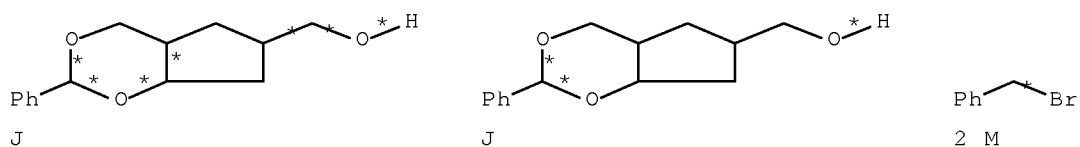
RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

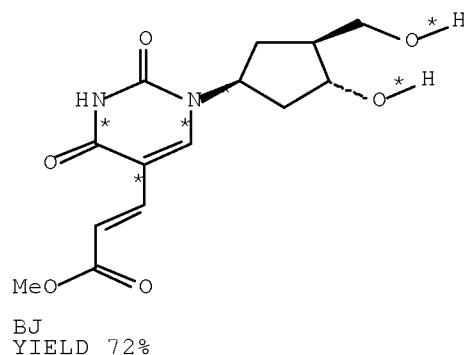
RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(235) OF 267 COMPOSED OF RX(4), RX(6), RX(8), RX(10), RX(12), RX(14), RX(16),  
 RX(18), RX(20), RX(22), RX(24), RX(26)  
 RX(235) 2 J + 2 M + 2 T + 2 Y + AV + BF ==>  
 BJ



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12  
STEPS  
→



RX(4)	RCT J 108275-94-1, M 100-39-0
	RGT O 7693-26-7 KH
	PRO N 120905-28-4
	SOL 109-99-9 THF
RX(6)	RCT N 120905-28-4
	RGT Q 7664-93-9 H2SO4
	PRO S 120963-35-1
	SOL 7732-18-5 Water
RX(8)	RCT S 120963-35-1, T 98-88-4
	RGT V 110-86-1 Pyridine
	PRO X 120963-36-2
	SOL 75-09-2 CH2Cl2
RX(10)	RCT X 120963-36-2, Y 124-63-0
	RGT AA 121-44-8 Et3N
	PRO AB 120963-37-3
	SOL 75-09-2 CH2Cl2
RX(12)	RCT AB 120963-37-3
	RGT AE 3396-11-0 Cs(OAc)2
	PRO AG 120963-38-4, AH 120905-31-9
	SOL 67-68-5 DMSO
RX(14)	RCT AG 120963-38-4
	RGT AJ 1333-74-0 H2
	PRO AM 120963-39-5
	CAT 7440-05-3 Pd
	SOL 64-17-5 EtOH
RX(16)	RCT AM 120963-39-5
	RGT AO 20039-37-6 PDC
	PRO AP 120963-40-8
	SOL 68-12-2 DMF
RX(18)	RCT AP 120963-40-8

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

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STAGE(2)

RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AX 120963-42-0  
SOL 75-09-2 CH2Cl2

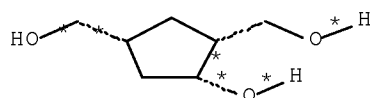
RX(22) RCT AX 120963-42-0  
RGT AS 7664-41-7 NH3  
PRO AZ 120963-44-2  
SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BE 120963-45-3  
SOL 123-91-1 Dioxane

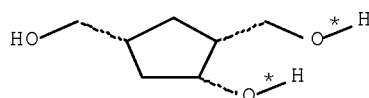
RX(26) RCT BE 120963-45-3, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BJ 120963-47-5  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(236) OF 267 COMPOSED OF RX(3), RX(4), RX(6), RX(8), RX(10), RX(12), RX(14),  
RX(16), RX(18), RX(20), RX(22), RX(24), RX(26)

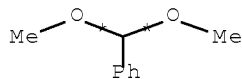
RX(236) 2 B + I + 2 M + 2 T + 2 Y + AV + BF  
====> BJ



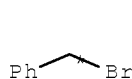
B



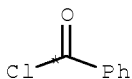
B



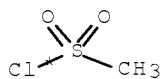
I



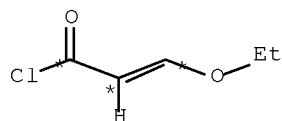
2 M



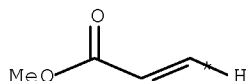
2 T



2 Y

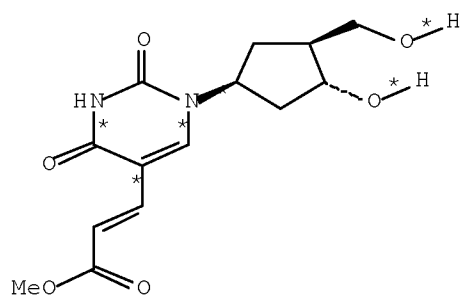


AV



BF

13  
STEPS  
→



BJ  
YIELD 72%

RX(3)	RCT	B 114129-19-0, I 1125-88-8
	RGT	K 16872-11-0 HBF <sub>4</sub>
	PRO	J 108275-94-1
	SOL	68-12-2 DMF
RX(4)	RCT	J 108275-94-1, M 100-39-0
	RGT	O 7693-26-7 KH
	PRO	N 120905-28-4
	SOL	109-99-9 THF
RX(6)	RCT	N 120905-28-4
	RGT	Q 7664-93-9 H <sub>2</sub> SO <sub>4</sub>
	PRO	S 120963-35-1
	SOL	7732-18-5 Water
RX(8)	RCT	S 120963-35-1, T 98-88-4
	RGT	V 110-86-1 Pyridine
	PRO	X 120963-36-2
	SOL	75-09-2 CH <sub>2</sub> Cl <sub>2</sub>
RX(10)	RCT	X 120963-36-2, Y 124-63-0
	RGT	AA 121-44-8 Et <sub>3</sub> N
	PRO	AB 120963-37-3
	SOL	75-09-2 CH <sub>2</sub> Cl <sub>2</sub>
RX(12)	RCT	AB 120963-37-3
	RGT	AE 3396-11-0 Cs(OAc) <sub>2</sub>
	PRO	AG 120963-38-4, AH 120905-31-9
	SOL	67-68-5 DMSO
RX(14)	RCT	AG 120963-38-4
	RGT	AJ 1333-74-0 H <sub>2</sub>
	PRO	AM 120963-39-5
	CAT	7440-05-3 Pd
	SOL	64-17-5 EtOH
RX(16)	RCT	AM 120963-39-5

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RGT AO 20039-37-6 PDC  
 PRO AP 120963-40-8  
 SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3  
 SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH2Cl2

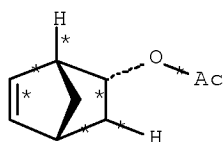
RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

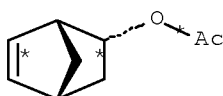
RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(237) OF 267 COMPOSED OF RX(1), RX(3), RX(4), RX(6), RX(8), RX(10), RX(12),  
 RX(14), RX(16), RX(18), RX(20), RX(22), RX(24), RX(26)

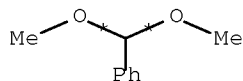
RX(237) 2 A + I + 2 M + 2 T + 2 Y + AV + BF  
 ==> BJ



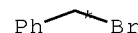
A



A

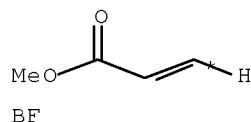
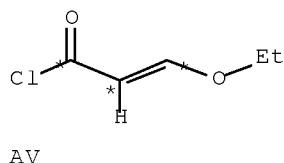
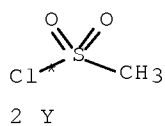
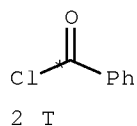


I

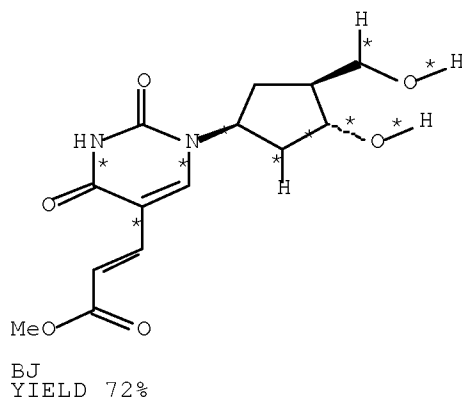


2 M

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14  
STEPS  
→



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RX(1)      RCT  A 112836-09-6

            STAGE(1)
              RGT  C 10028-15-6 Ozone
              SOL  67-56-1 MeOH

            STAGE(2)
              RGT  D 16853-85-3 LiAlH4
              SOL  109-99-9 THF

PRO  B 114129-19-0

RX(3)      RCT  B 114129-19-0, I 1125-88-8
              RGT  K 16872-11-0 HBF4
              PRO  J 108275-94-1
              SOL  68-12-2 DMF

RX(4)      RCT  J 108275-94-1, M 100-39-0
              RGT  O 7693-26-7 KH
              PRO  N 120905-28-4
              SOL  109-99-9 THF

RX(6)      RCT  N 120905-28-4
              RGT  Q 7664-93-9 H2SO4
              PRO  S 120963-35-1
              SOL  7732-18-5 Water

RX(8)      RCT  S 120963-35-1, T 98-88-4
              RGT  V 110-86-1 Pyridine
  
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PRO X 120963-36-2  
SOL 75-09-2 CH2Cl2

RX(10) RCT X 120963-36-2, Y 124-63-0  
RGT AA 121-44-8 Et3N  
PRO AB 120963-37-3  
SOL 75-09-2 CH2Cl2

RX(12) RCT AB 120963-37-3  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AG 120963-38-4, AH 120905-31-9  
SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
RGT AJ 1333-74-0 H2  
PRO AM 120963-39-5  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
RGT AO 20039-37-6 PDC  
PRO AP 120963-40-8  
SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)  
RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)  
RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AX 120963-42-0  
SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
RGT AS 7664-41-7 NH3  
PRO AZ 120963-44-2  
SOL 7732-18-5 Water

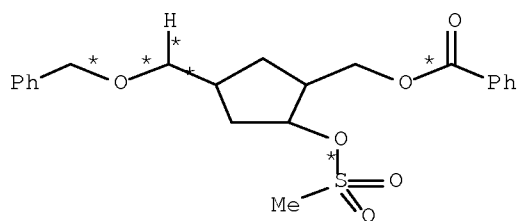
RX(24) RCT AZ 120963-44-2  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BE 120963-45-3  
SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BJ 120963-47-5  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

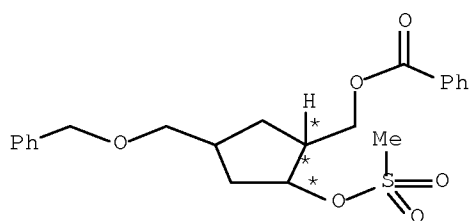
RX(238) OF 267 COMPOSED OF RX(11), RX(13), RX(15), RX(17), RX(19), RX(21),  
RX(23), RX(25), RX(27)

RX(238) 2 Z + AV + BF ==> BK

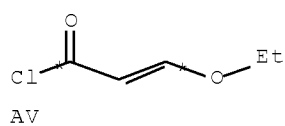
10/569486



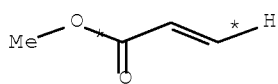
Z



Z

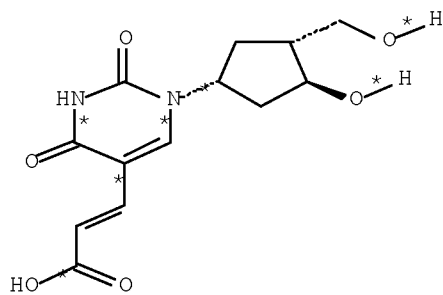


AV



BF

9  
STEPS  
→



BK

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H<sub>2</sub>  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF



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RX(17) RCT AN 120905-33-1

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3

SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7

RGT V 110-86-1 Pyridine

PRO AW 120905-35-3

SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3

RGT AS 7664-41-7 NH3

PRO AY 120963-43-1

SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1

RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3

PRO BA 114179-59-8

SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3

RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N

PRO BG 120963-46-4

CAT 3375-31-3 Pd(OAc)2

SOL 123-91-1 Dioxane

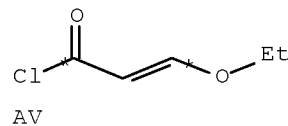
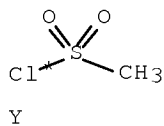
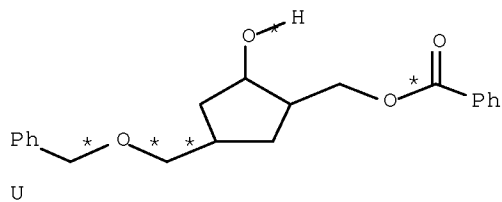
RX(27) RCT BG 120963-46-4

RGT BL 1310-58-3 KOH

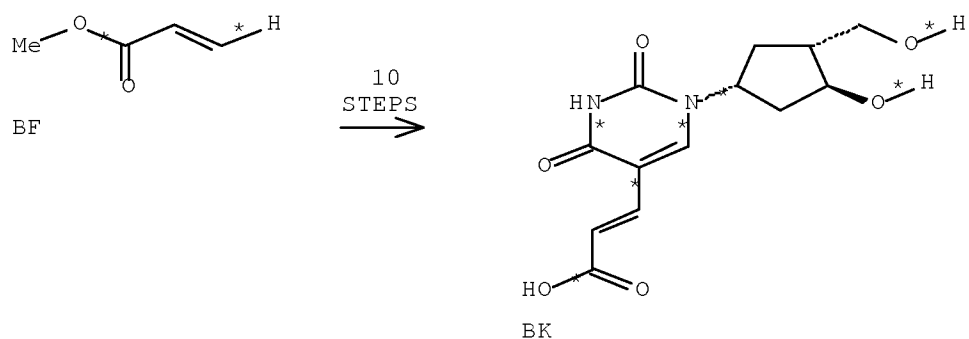
PRO BK 120963-48-6

RX(239) OF 267 COMPOSED OF RX(9), RX(11), RX(13), RX(15), RX(17), RX(19),  
RX(21), RX(23), RX(25), RX(27)

RX(239) U + Y + AV + BF ==> BK



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RX(9)	RCT	U 120236-99-9, Y 124-63-0
	RGT	AA 121-44-8 Et3N
	PRO	Z 116142-70-2
	SOL	75-09-2 CH2Cl2
RX(11)	RCT	Z 116142-70-2
	RGT	AE 3396-11-0 Cs(OAc)2
	PRO	AC 120905-29-5, AD 120905-30-8
	SOL	67-68-5 DMSO
RX(13)	RCT	AC 120905-29-5
	RGT	AJ 1333-74-0 H2
	PRO	AI 120905-32-0
	CAT	7440-05-3 Pd
	SOL	64-17-5 EtOH
RX(15)	RCT	AI 120905-32-0
	RGT	AO 20039-37-6 PDC
	PRO	AN 120905-33-1
	SOL	68-12-2 DMF
RX(17)	RCT	AN 120905-33-1
	STAGE(1)	
	RGT	AR 26386-88-9 (PhO)2P(O)N3
	SOL	71-43-2 Benzene
	STAGE(2)	
	RGT	AS 7664-41-7 NH3
	PRO	AQ 120905-34-2
RX(19)	RCT	AQ 120905-34-2, AV 6191-99-7
	RGT	V 110-86-1 Pyridine
	PRO	AW 120905-35-3
	SOL	75-09-2 CH2Cl2
RX(21)	RCT	AW 120905-35-3
	RGT	AS 7664-41-7 NH3
	PRO	AY 120963-43-1
	SOL	7732-18-5 Water
RX(23)	RCT	AY 120963-43-1

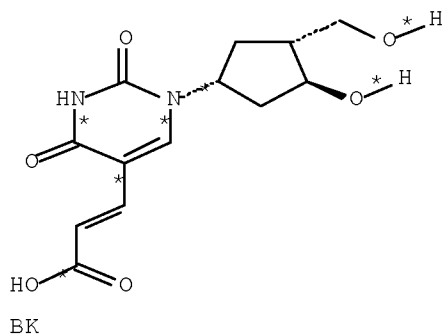
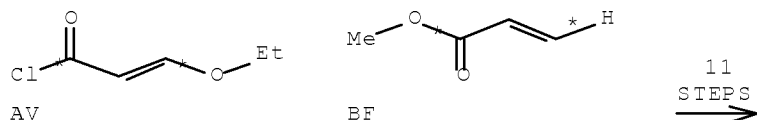
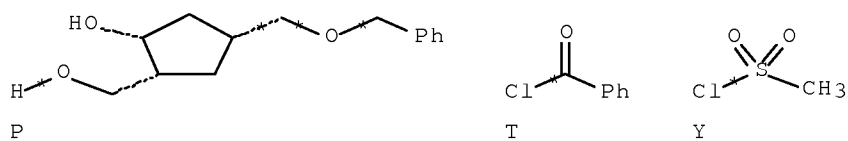
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RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BA 114179-59-8  
 SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BG 120963-46-4  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(27) RCT BG 120963-46-4  
 RGT BL 1310-58-3 KOH  
 PRO BK 120963-48-6

RX(240) OF 267 COMPOSED OF RX(7), RX(9), RX(11), RX(13), RX(15), RX(17),  
 RX(19), RX(21), RX(23), RX(25), RX(27)  
 RX(240) P + T + Y + AV + BF ==> BK



RX(7) RCT P 120236-98-8, T 98-88-4  
 RGT V 110-86-1 Pyridine  
 PRO U 120236-99-9

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SOL 75-09-2 CH2Cl2

RX(9) RCT U 120236-99-9, Y 124-63-0  
RGT AA 121-44-8 Et3N  
PRO Z 116142-70-2  
SOL 75-09-2 CH2Cl2

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H2  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)  
RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)  
RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

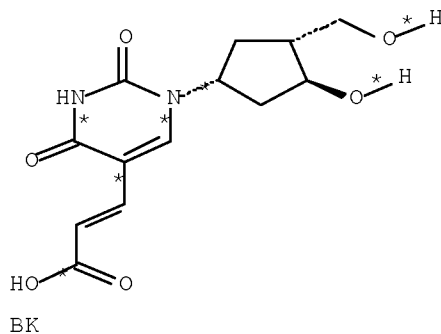
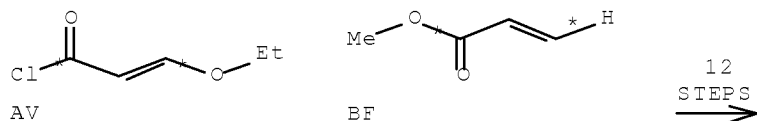
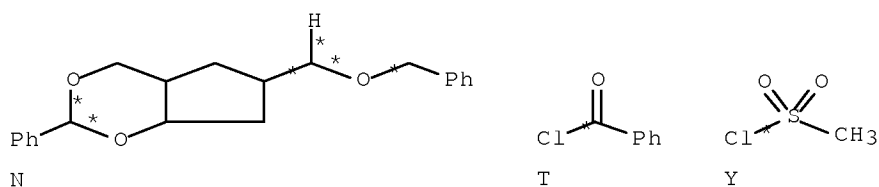
RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(27) RCT BG 120963-46-4  
RGT BL 1310-58-3 KOH  
PRO BK 120963-48-6

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RX(241) OF 267 COMPOSED OF RX(5), RX(7), RX(9), RX(11), RX(13), RX(15), RX(17),  
RX(19), RX(21), RX(23), RX(25), RX(27)

RX(241) N + T + Y + AV + BF ==> BK



RX(5)	RCT	N 120905-28-4
	RGT	Q 7664-93-9 H2SO4
	PRO	P 120236-98-8
	SOL	7732-18-5 Water
RX(7)	RCT	P 120236-98-8, T 98-88-4
	RGT	V 110-86-1 Pyridine
	PRO	U 120236-99-9
	SOL	75-09-2 CH2Cl2
RX(9)	RCT	U 120236-99-9, Y 124-63-0
	RGT	AA 121-44-8 Et3N
	PRO	Z 116142-70-2
	SOL	75-09-2 CH2Cl2
RX(11)	RCT	Z 116142-70-2

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RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H<sub>2</sub>  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)

RGT AR 26386-88-9 (PhO)<sub>2</sub>P(O)N<sub>3</sub>  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH<sub>3</sub>

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH<sub>3</sub>  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I<sub>2</sub>, BC 7697-37-2 HNO<sub>3</sub>  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

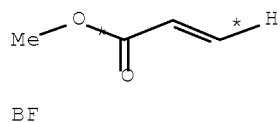
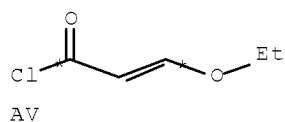
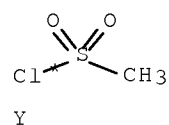
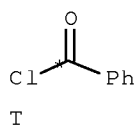
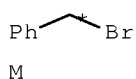
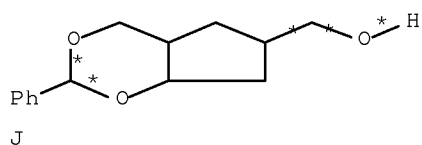
RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh<sub>3</sub>, AA 121-44-8 Et<sub>3</sub>N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)<sub>2</sub>  
SOL 123-91-1 Dioxane

RX(27) RCT BG 120963-46-4  
RGT BL 1310-58-3 KOH  
PRO BK 120963-48-6

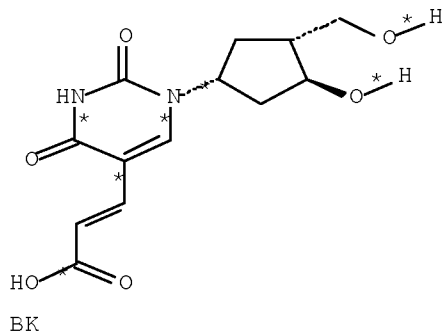
RX(242) OF 267 COMPOSED OF RX(4), RX(5), RX(7), RX(9), RX(11), RX(13), RX(15),  
RX(17), RX(19), RX(21), RX(23), RX(25), RX(27)

RX(242) J + M + T + Y + AV + BF ==>  
BK

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13  
STEPS  
→



RX(4) RCT J 108275-94-1, M 100-39-0  
RGT O 7693-26-7 KH  
PRO N 120905-28-4  
SOL 109-99-9 THF

RX(5) RCT N 120905-28-4  
RGT Q 7664-93-9 H2SO4  
PRO P 120236-98-8  
SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO U 120236-99-9  
SOL 75-09-2 CH2Cl2

RX(9) RCT U 120236-99-9, Y 124-63-0  
RGT AA 121-44-8 Et3N  
PRO Z 116142-70-2  
SOL 75-09-2 CH2Cl2

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AC 120905-29-5, AD 120905-30-8

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```
SOL  67-68-5 DMSO

RX(13)  RCT  AC 120905-29-5
        RGT  AJ 1333-74-0 H2
        PRO  AI 120905-32-0
        CAT  7440-05-3 Pd
        SOL  64-17-5 EtOH

RX(15)  RCT  AI 120905-32-0
        RGT  AO 20039-37-6 PDC
        PRO  AN 120905-33-1
        SOL  68-12-2 DMF

RX(17)  RCT  AN 120905-33-1

        STAGE(1)
          RGT  AR 26386-88-9 (PhO)2P(O)N3
          SOL  71-43-2 Benzene

        STAGE(2)
          RGT  AS 7664-41-7 NH3

        PRO  AQ 120905-34-2

RX(19)  RCT  AQ 120905-34-2, AV 6191-99-7
        RGT  V 110-86-1 Pyridine
        PRO  AW 120905-35-3
        SOL  75-09-2 CH2Cl2

RX(21)  RCT  AW 120905-35-3
        RGT  AS 7664-41-7 NH3
        PRO  AY 120963-43-1
        SOL  7732-18-5 Water

RX(23)  RCT  AY 120963-43-1
        RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
        PRO  BA 114179-59-8
        SOL  123-91-1 Dioxane

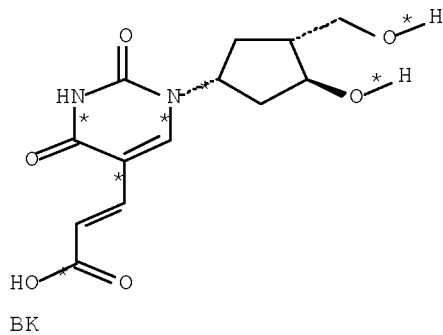
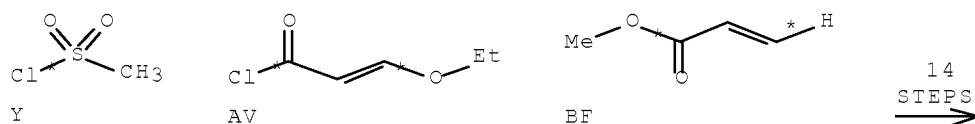
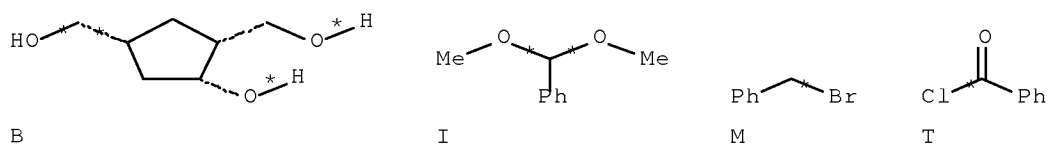
RX(25)  RCT  BA 114179-59-8, BF 96-33-3
        RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
        PRO  BG 120963-46-4
        CAT  3375-31-3 Pd(OAc)2
        SOL  123-91-1 Dioxane

RX(27)  RCT  BG 120963-46-4
        RGT  BL 1310-58-3 KOH
        PRO  BK 120963-48-6

RX(243) OF 267 COMPOSED OF RX(3), RX(4), RX(5), RX(7), RX(9), RX(11), RX(13),
        RX(15), RX(17), RX(19), RX(21), RX(23), RX(25), RX(27)
RX(243)  B + I + M + T + Y + AV + BF ==>
        EK
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RX(3) RCT B 114129-19-0, I 1125-88-8  
 RGT K 16872-11-0 HBF<sub>4</sub>  
 PRO J 108275-94-1  
 SOL 68-12-2 DMF

RX(4) RCT J 108275-94-1, M 100-39-0  
 RGT O 7693-26-7 KH  
 PRO N 120905-28-4  
 SOL 109-99-9 THF

RX(5) RCT N 120905-28-4  
 RGT Q 7664-93-9 H<sub>2</sub>SO<sub>4</sub>  
 PRO P 120236-98-8  
 SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4  
 RGT V 110-86-1 Pyridine  
 PRO U 120236-99-9  
 SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(9) RCT U 120236-99-9, Y 124-63-0  
 RGT AA 121-44-8 Et<sub>3</sub>N  
 PRO Z 116142-70-2

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```
SOL 75-09-2 CH2Cl2

RX(11)  RCT  Z 116142-70-2
        RGT  AE 3396-11-0 Cs(OAc)2
        PRO  AC 120905-29-5, AD 120905-30-8
        SOL  67-68-5 DMSO

RX(13)  RCT  AC 120905-29-5
        RGT  AJ 1333-74-0 H2
        PRO  AI 120905-32-0
        CAT  7440-05-3 Pd
        SOL  64-17-5 EtOH

RX(15)  RCT  AI 120905-32-0
        RGT  AO 20039-37-6 PDC
        PRO  AN 120905-33-1
        SOL  68-12-2 DMF

RX(17)  RCT  AN 120905-33-1

        STAGE(1)
            RGT  AR 26386-88-9 (PhO)2P(O)N3
            SOL  71-43-2 Benzene

        STAGE(2)
            RGT  AS 7664-41-7 NH3

        PRO  AQ 120905-34-2

RX(19)  RCT  AQ 120905-34-2, AV 6191-99-7
        RGT  V 110-86-1 Pyridine
        PRO  AW 120905-35-3
        SOL  75-09-2 CH2Cl2

RX(21)  RCT  AW 120905-35-3
        RGT  AS 7664-41-7 NH3
        PRO  AY 120963-43-1
        SOL  7732-18-5 Water

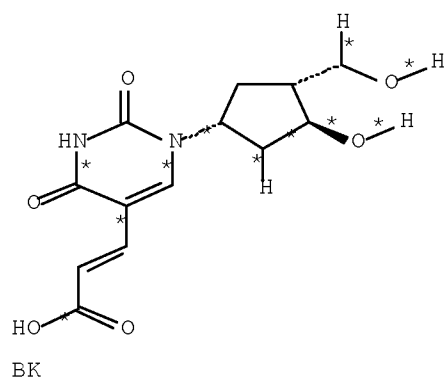
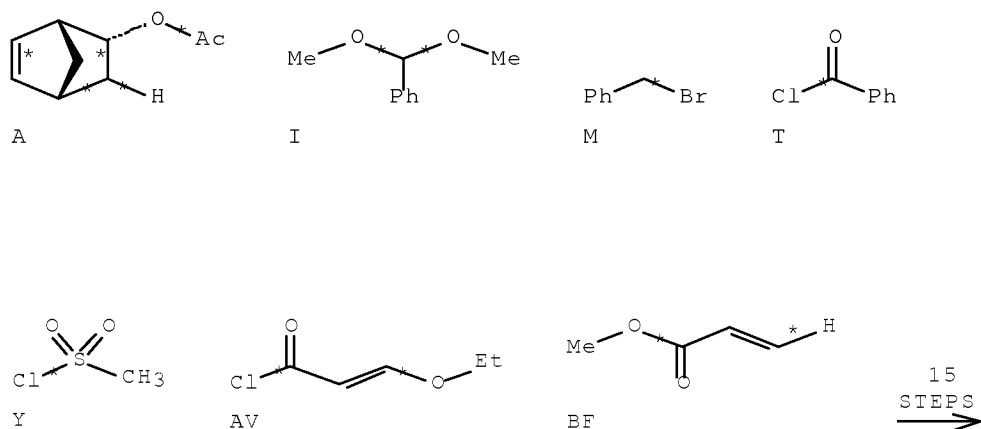
RX(23)  RCT  AY 120963-43-1
        RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
        PRO  BA 114179-59-8
        SOL  123-91-1 Dioxane

RX(25)  RCT  BA 114179-59-8, BF 96-33-3
        RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
        PRO  BG 120963-46-4
        CAT  3375-31-3 Pd(OAc)2
        SOL  123-91-1 Dioxane

RX(27)  RCT  BG 120963-46-4
        RGT  BL 1310-58-3 KOH
        PRO  BK 120963-48-6

RX(244) OF 267 COMPOSED OF RX(1), RX(3), RX(4), RX(5), RX(7), RX(9), RX(11),
        RX(13), RX(15), RX(17), RX(19), RX(21), RX(23), RX(25), RX(27)
RX(244)  A + I + M + T + Y + AV + BF ==>
        BK
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```

RX(1)      RCT  A 112836-09-6

            STAGE(1)
            RGT  C 10028-15-6 Ozone
            SOL  67-56-1 MeOH

            STAGE(2)
            RGT  D 16853-85-3 LiAlH4
            SOL  109-99-9 THF

            PRO  B 114129-19-0

RX(3)      RCT  B 114129-19-0, I 1125-88-8
            RGT  K 16872-11-0 HBF4
            PRO  J 108275-94-1
            SOL  68-12-2 DMF

RX(4)      RCT  J 108275-94-1, M 100-39-0
            RGT  O 7693-26-7 KH
            PRO  N 120905-28-4
            SOL  109-99-9 THF
  
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RX(5) RCT N 120905-28-4  
RGT Q 7664-93-9 H2SO4  
PRO P 120236-98-8  
SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO U 120236-99-9  
SOL 75-09-2 CH2Cl2

RX(9) RCT U 120236-99-9, Y 124-63-0  
RGT AA 121-44-8 Et3N  
PRO Z 116142-70-2  
SOL 75-09-2 CH2Cl2

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H2  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)  
RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)  
RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N

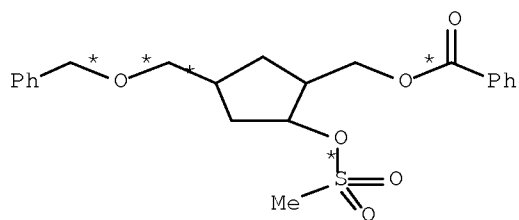
10/569486

PRO BG 120963-46-4  
 CAT 3375-31-3 Pd(OAc)<sub>2</sub>  
 SOL 123-91-1 Dioxane

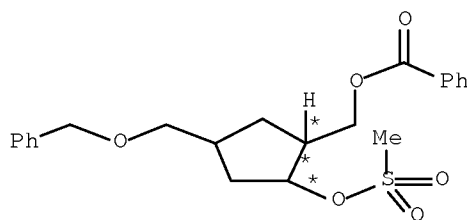
RX(27) RCT BG 120963-46-4  
 RGT BL 1310-58-3 KOH  
 PRO BK 120963-48-6

RX(245) OF 267 COMPOSED OF RX(12), RX(14), RX(16), RX(18), RX(20), RX(22),  
 RX(24), RX(26), RX(28)

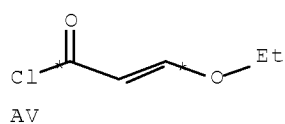
RX(245) 2 AB + AV + BF ==> BM



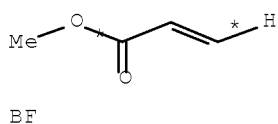
AB



AB

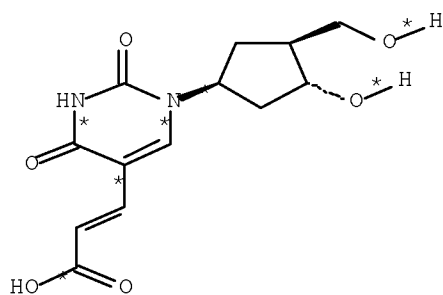


AV



BF

9  
 STEPS  
 →



BM

RX(12) RCT AB 120963-37-3  
 RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
 PRO AG 120963-38-4, AH 120905-31-9  
 SOL 67-68-5 DMSO

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RX(14) RCT AG 120963-38-4  
RGT AJ 1333-74-0 H2  
PRO AM 120963-39-5  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
RGT AO 20039-37-6 PDC  
PRO AP 120963-40-8  
SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AX 120963-42-0  
SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
RGT AS 7664-41-7 NH3  
PRO AZ 120963-44-2  
SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BE 120963-45-3  
SOL 123-91-1 Dioxane

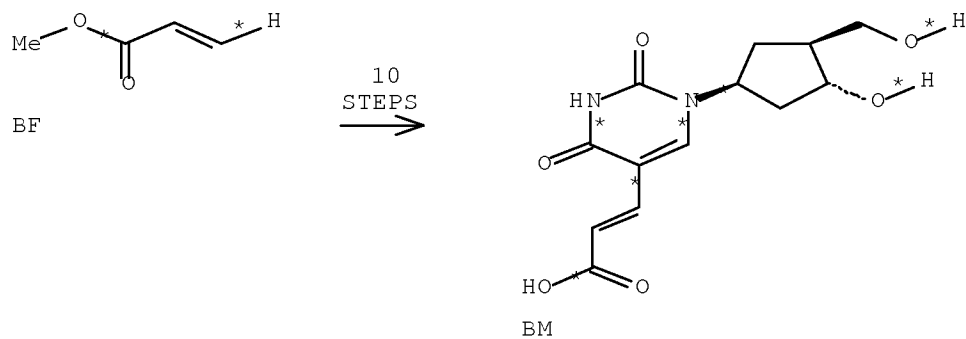
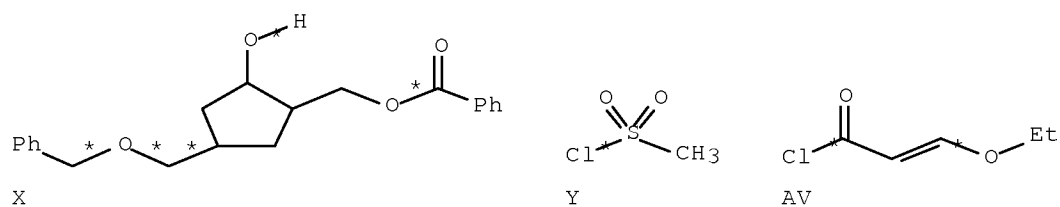
RX(26) RCT BE 120963-45-3, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BJ 120963-47-5  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
RGT BL 1310-58-3 KOH  
PRO BM 120963-49-7

RX(246) OF 267 COMPOSED OF RX(10), RX(12), RX(14), RX(16), RX(18), RX(20),  
RX(22), RX(24), RX(26), RX(28)

RX(246) X + Y + AV + BF ==> BM

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RX(10) RCT X 120963-36-2, Y 124-63-0  
 RGT AA 121-44-8 Et3N  
 PRO AB 120963-37-3  
 SOL 75-09-2 CH2Cl2

RX(12) RCT AB 120963-37-3  
 RGT AE 3396-11-0 Cs(OAc)2  
 PRO AG 120963-38-4, AH 120905-31-9  
 SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
 RGT AJ 1333-74-0 H2  
 PRO AM 120963-39-5  
 CAT 7440-05-3 Pd  
 SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
 RGT AO 20039-37-6 PDC  
 PRO AP 120963-40-8  
 SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)  
 RGT AR 26386-88-9 (PhO)2P(O)N3  
 SOL 71-43-2 Benzene

STAGE(2)  
 RGT AS 7664-41-7 NH3

10/569486

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

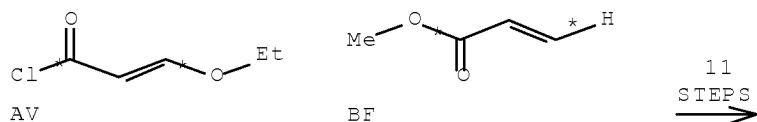
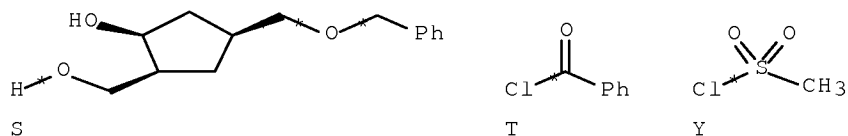
RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

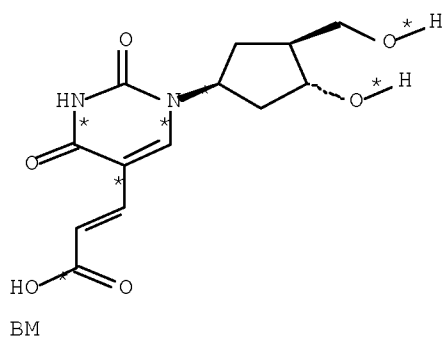
RX(247) OF 267 COMPOSED OF RX(8), RX(10), RX(12), RX(14), RX(16), RX(18),  
 RX(20), RX(22), RX(24), RX(26), RX(28)

RX(247) S + T + Y + AV + BF ==> BM





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RX(8) RCT S 120963-35-1, T 98-88-4  
 RGT V 110-86-1 Pyridine  
 PRO X 120963-36-2  
 SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(10) RCT X 120963-36-2, Y 124-63-0  
 RGT AA 121-44-8 Et<sub>3</sub>N  
 PRO AB 120963-37-3  
 SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(12) RCT AB 120963-37-3  
 RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
 PRO AG 120963-38-4, AH 120905-31-9  
 SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
 RGT AJ 1333-74-0 H<sub>2</sub>  
 PRO AM 120963-39-5  
 CAT 7440-05-3 Pd  
 SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
 RGT AO 20039-37-6 PDC  
 PRO AP 120963-40-8  
 SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)

RGT AR 26386-88-9 (PhO)<sub>2</sub>P(O)N<sub>3</sub>  
 SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH<sub>3</sub>

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(22) RCT AX 120963-42-0

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RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

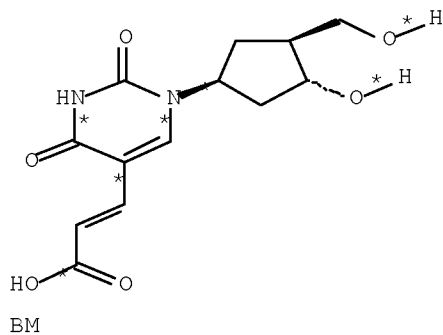
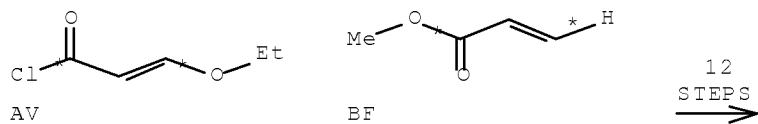
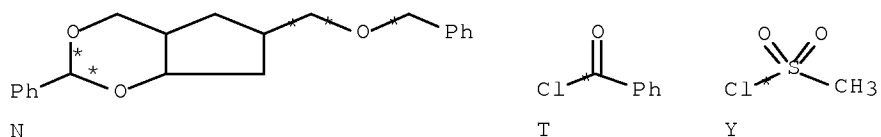
RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

RX(248) OF 267 COMPOSED OF RX(6), RX(8), RX(10), RX(12), RX(14), RX(16),  
 RX(18), RX(20), RX(22), RX(24), RX(26), RX(28)

RX(248) N + T + Y + AV + BF ==> BM



RX(6) RCT N 120905-28-4  
 RGT Q 7664-93-9 H2SO4  
 PRO S 120963-35-1  
 SOL 7732-18-5 Water

RX(8) RCT S 120963-35-1, T 98-88-4  
 RGT V 110-86-1 Pyridine  
 PRO X 120963-36-2  
 SOL 75-09-2 CH2Cl2

RX(10) RCT X 120963-36-2, Y 124-63-0  
 RGT AA 121-44-8 Et3N  
 PRO AB 120963-37-3  
 SOL 75-09-2 CH2Cl2

RX(12) RCT AB 120963-37-3  
 RGT AE 3396-11-0 Cs(OAc)2  
 PRO AG 120963-38-4, AH 120905-31-9  
 SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
 RGT AJ 1333-74-0 H2  
 PRO AM 120963-39-5  
 CAT 7440-05-3 Pd  
 SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
 RGT AO 20039-37-6 PDC  
 PRO AP 120963-40-8  
 SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)  
 RGT AR 26386-88-9 (PhO)2P(O)N3  
 SOL 71-43-2 Benzene

STAGE(2)  
 RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3

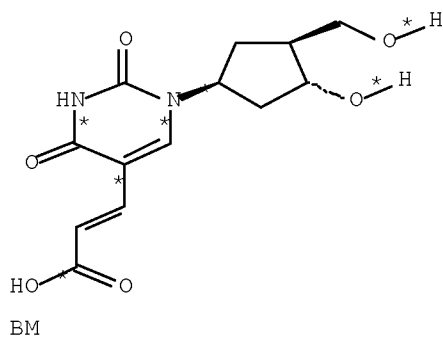
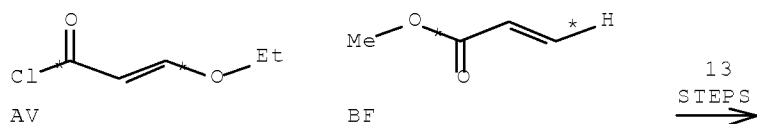
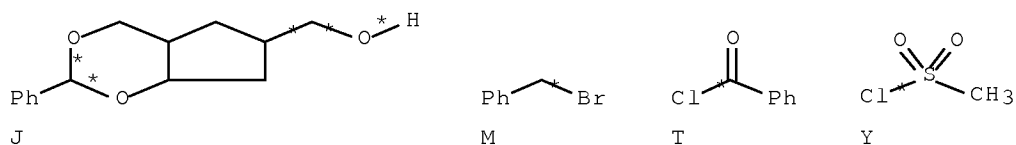
10/569486

RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

RX(249) OF 267 COMPOSED OF RX(4), RX(6), RX(8), RX(10), RX(12), RX(14), RX(16),  
 RX(18), RX(20), RX(22), RX(24), RX(26), RX(28)

RX(249) J + M + T + Y + AV + BF ==>  
 EM



RX(4) RCT J 108275-94-1, M 100-39-0  
 RGT O 7693-26-7 KH  
 PRO N 120905-28-4  
 SOL 109-99-9 THF

RX(6) RCT N 120905-28-4  
 RGT Q 7664-93-9 H2SO4

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PRO S 120963-35-1  
SOL 7732-18-5 Water

RX(8) RCT S 120963-35-1, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO X 120963-36-2  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(10) RCT X 120963-36-2, Y 124-63-0  
RGT AA 121-44-8 Et<sub>3</sub>N  
PRO AB 120963-37-3  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(12) RCT AB 120963-37-3  
RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
PRO AG 120963-38-4, AH 120905-31-9  
SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
RGT AJ 1333-74-0 H<sub>2</sub>  
PRO AM 120963-39-5  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
RGT AO 20039-37-6 PDC  
PRO AP 120963-40-8  
SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)

RGT AR 26386-88-9 (PhO)<sub>2</sub>P(O)N<sub>3</sub>  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH<sub>3</sub>

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AX 120963-42-0  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(22) RCT AX 120963-42-0  
RGT AS 7664-41-7 NH<sub>3</sub>  
PRO AZ 120963-44-2  
SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
RGT BB 7553-56-2 I<sub>2</sub>, BC 7697-37-2 HNO<sub>3</sub>  
PRO BE 120963-45-3  
SOL 123-91-1 Dioxane

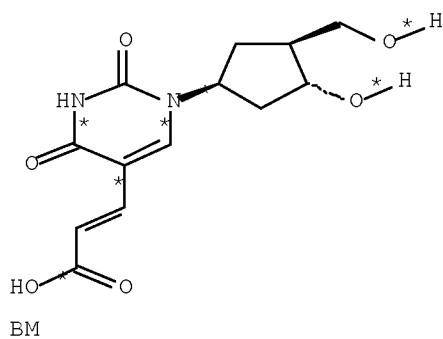
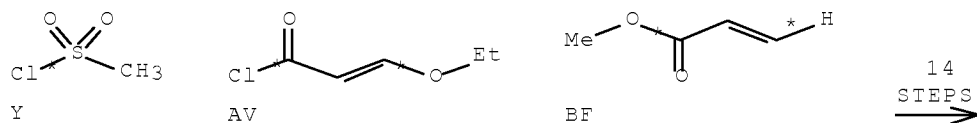
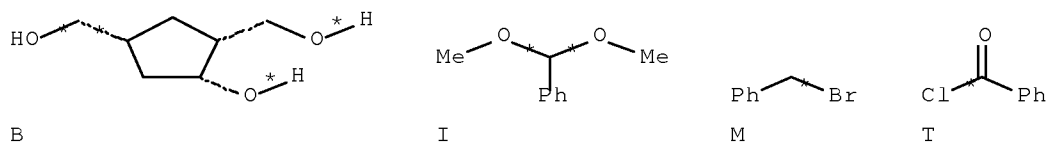
RX(26) RCT BE 120963-45-3, BF 96-33-3  
RGT BH 603-35-0 PPh<sub>3</sub>, AA 121-44-8 Et<sub>3</sub>N  
PRO BJ 120963-47-5  
CAT 3375-31-3 Pd(OAc)<sub>2</sub>  
SOL 123-91-1 Dioxane

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RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

RX(250) OF 267 COMPOSED OF RX(3), RX(4), RX(6), RX(8), RX(10), RX(12), RX(14),  
 RX(16), RX(18), RX(20), RX(22), RX(24), RX(26), RX(28)

RX(250) B + I + M + T + Y + AV + BF ==>  
 BM



RX(3) RCT B 114129-19-0, I 1125-88-8  
 RGT K 16872-11-0 HBF<sub>4</sub>  
 PRO J 108275-94-1  
 SOL 68-12-2 DMF

RX(4) RCT J 108275-94-1, M 100-39-0  
 RGT O 7693-26-7 KH  
 PRO N 120905-28-4  
 SOL 109-99-9 THF

RX(6) RCT N 120905-28-4  
 RGT Q 7664-93-9 H<sub>2</sub>SO<sub>4</sub>

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PRO S 120963-35-1  
SOL 7732-18-5 Water

RX(8) RCT S 120963-35-1, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO X 120963-36-2  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(10) RCT X 120963-36-2, Y 124-63-0  
RGT AA 121-44-8 Et<sub>3</sub>N  
PRO AB 120963-37-3  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(12) RCT AB 120963-37-3  
RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
PRO AG 120963-38-4, AH 120905-31-9  
SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
RGT AJ 1333-74-0 H<sub>2</sub>  
PRO AM 120963-39-5  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
RGT AO 20039-37-6 PDC  
PRO AP 120963-40-8  
SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)

RGT AR 26386-88-9 (PhO)<sub>2</sub>P(O)N<sub>3</sub>  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH<sub>3</sub>

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AX 120963-42-0  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(22) RCT AX 120963-42-0  
RGT AS 7664-41-7 NH<sub>3</sub>  
PRO AZ 120963-44-2  
SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
RGT BB 7553-56-2 I<sub>2</sub>, BC 7697-37-2 HNO<sub>3</sub>  
PRO BE 120963-45-3  
SOL 123-91-1 Dioxane

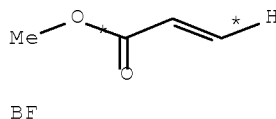
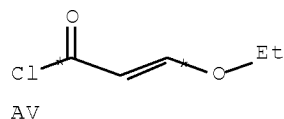
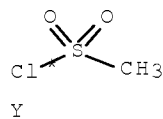
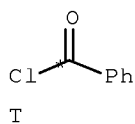
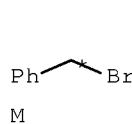
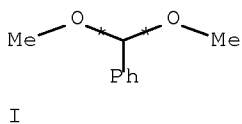
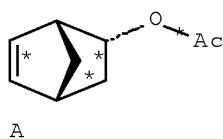
RX(26) RCT BE 120963-45-3, BF 96-33-3  
RGT BH 603-35-0 PPh<sub>3</sub>, AA 121-44-8 Et<sub>3</sub>N  
PRO BJ 120963-47-5  
CAT 3375-31-3 Pd(OAc)<sub>2</sub>  
SOL 123-91-1 Dioxane

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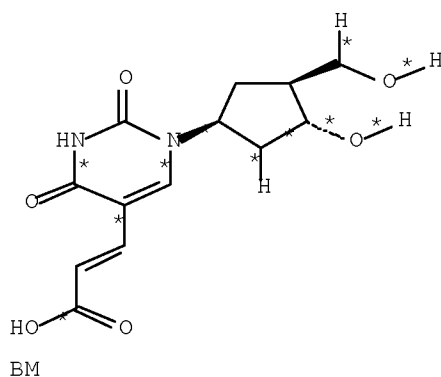
RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

RX(251) OF 267 COMPOSED OF RX(1), RX(3), RX(4), RX(6), RX(8), RX(10), RX(12),  
 RX(14), RX(16), RX(18), RX(20), RX(22), RX(24), RX(26), RX(28)

RX(251) A + I + M + T + Y + AV + BF ==>  
 BM



15  
 STEPS  
 >



RX(1) RCT A 112836-09-6

STAGE(1)

RGT C 10028-15-6 Ozone  
 SOL 67-56-1 MeOH

STAGE(2)

RGT D 16853-85-3 LiAlH4  
 SOL 109-99-9 THF



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PRO B 114129-19-0

RX(3) RCT B 114129-19-0, I 1125-88-8  
RGT K ~~16872-11-0~~ HBF<sub>4</sub>  
PRO J 108275-94-1  
SOL 68-12-2 DMF

RX(4) RCT J 108275-94-1, M 100-39-0  
RGT O 7693-26-7 KH  
PRO N 120905-28-4  
SOL 109-99-9 THF

RX(6) RCT N 120905-28-4  
RGT Q 7664-93-9 H<sub>2</sub>SO<sub>4</sub>  
PRO S 120963-35-1  
SOL 7732-18-5 Water

RX(8) RCT S 120963-35-1, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO X 120963-36-2  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(10) RCT X 120963-36-2, Y 124-63-0  
RGT AA 121-44-8 Et<sub>3</sub>N  
PRO AB 120963-37-3  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(12) RCT AB 120963-37-3  
RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
PRO AG 120963-38-4, AH 120905-31-9  
SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
RGT AJ 1333-74-0 H<sub>2</sub>  
PRO AM 120963-39-5  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
RGT AO 20039-37-6 PDC  
PRO AP 120963-40-8  
SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)  
RGT AR 26386-88-9 (PhO)<sub>2</sub>P(O)N<sub>3</sub>  
SOL 71-43-2 Benzene

STAGE(2)  
RGT AS 7664-41-7 NH<sub>3</sub>

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AX 120963-42-0  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(22) RCT AX 120963-42-0

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RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

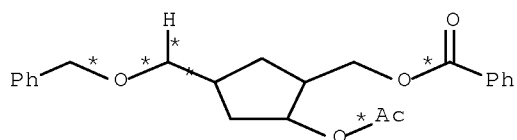
RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

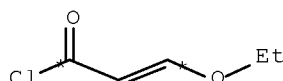
RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

RX(252) OF 267 COMPOSED OF RX(13), RX(15), RX(17), RX(19), RX(21), RX(23),  
 RX(25), RX(27), RX(29)

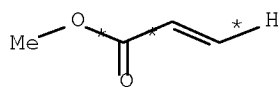
RX(252) AC + AV + BF ==> BN



AC

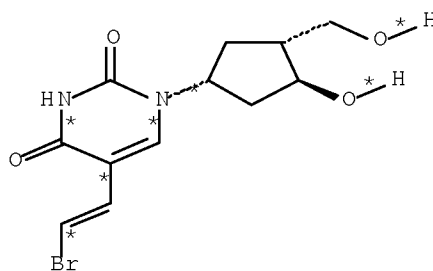


AV



BF

9  
 STEPS  
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BN

RX(13) RCT AC 120905-29-5  
 RGT AJ 1333-74-0 H2  
 PRO AI 120905-32-0  
 CAT 7440-05-3 Pd  
 SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
 RGT AO 20039-37-6 PDC

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PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

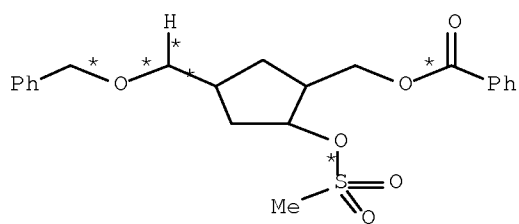
RX(27) RCT BG 120963-46-4  
RGT BL 1310-58-3 KOH  
PRO BK 120963-48-6

RX(29) RCT BK 120963-48-6  
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
PRO BN 95463-56-2  
SOL 68-12-2 DMF

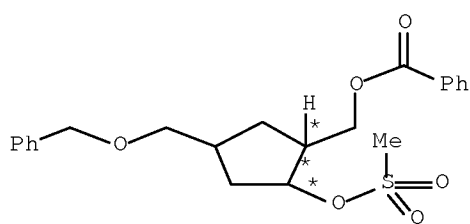
RX(253) OF 267 COMPOSED OF RX(11), RX(13), RX(15), RX(17), RX(19), RX(21),  
RX(23), RX(25), RX(27), RX(29)

RX(253) 2 Z + AV + BF ==> BN

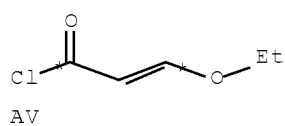
10/569486



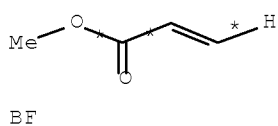
Z



Z

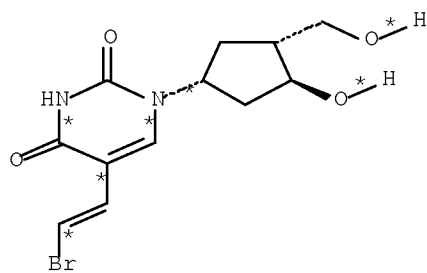


AV



BF

10  
STEPS  
→



BN

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H2  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)

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RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

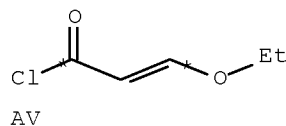
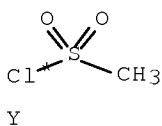
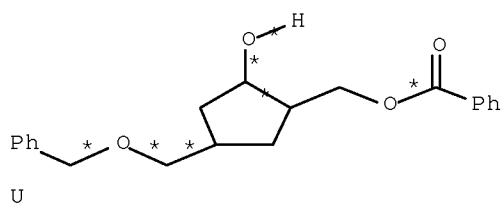
RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(27) RCT BG 120963-46-4  
RGT BL 1310-58-3 KOH  
PRO BK 120963-48-6

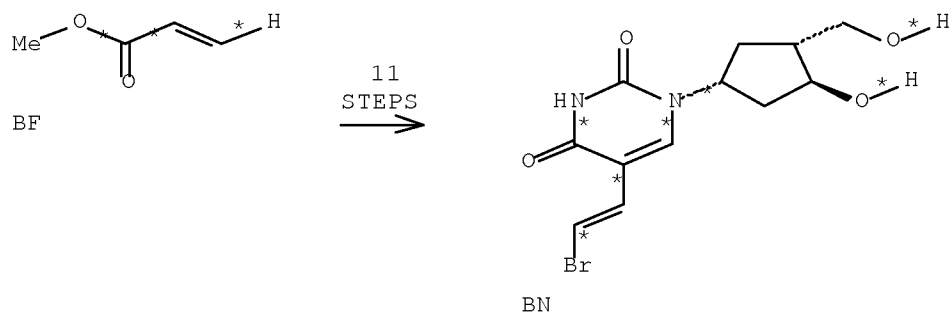
RX(29) RCT BK 120963-48-6  
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
PRO BN 95463-56-2  
SOL 68-12-2 DMF

RX(254) OF 267 COMPOSED OF RX(9), RX(11), RX(13), RX(15), RX(17), RX(19),  
RX(21), RX(23), RX(25), RX(27), RX(29)

RX(254) U + Y + AV + BF ==> BN



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RX(9) RCT U 120236-99-9, Y 124-63-0  
RGT AA 121-44-8 Et3N  
PRO Z 116142-70-2  
SOL 75-09-2 CH2Cl2

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H2  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)  
RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)  
RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3

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PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

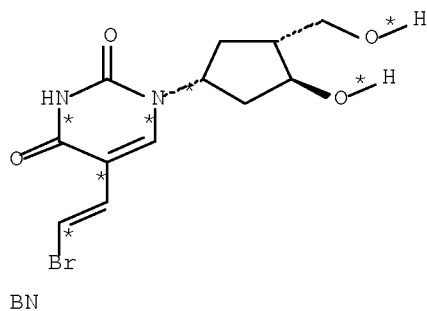
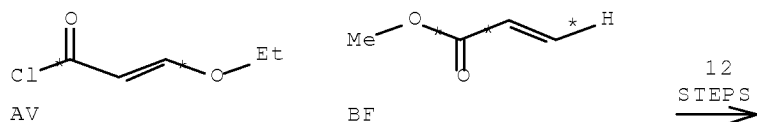
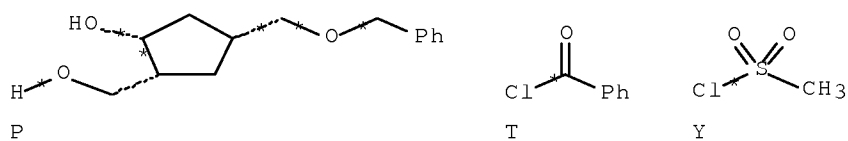
RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(27) RCT BG 120963-46-4  
RGT BL 1310-58-3 KOH  
PRO BK 120963-48-6

RX(29) RCT BK 120963-48-6  
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
PRO BN 95463-56-2  
SOL 68-12-2 DMF

RX(255) OF 267 COMPOSED OF RX(7), RX(9), RX(11), RX(13), RX(15), RX(17),  
RX(19), RX(21), RX(23), RX(25), RX(27), RX(29)

RX(255) P + T + Y + AV + BF ==> BN



RX(7) RCT P 120236-98-8, T 98-88-4

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RGT V 110-86-1 Pyridine  
PRO U 120236-99-9  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(9) RCT U 120236-99-9, Y 124-63-0  
RGT AA 121-44-8 Et<sub>3</sub>N  
PRO Z 116142-70-2  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H<sub>2</sub>  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)

RGT AR 26386-88-9 (PhO)<sub>2</sub>P(O)N<sub>3</sub>  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH<sub>3</sub>

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH<sub>3</sub>  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I<sub>2</sub>, BC 7697-37-2 HNO<sub>3</sub>  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh<sub>3</sub>, AA 121-44-8 Et<sub>3</sub>N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)<sub>2</sub>  
SOL 123-91-1 Dioxane

RX(27) RCT BG 120963-46-4  
RGT BL 1310-58-3 KOH  
PRO BK 120963-48-6

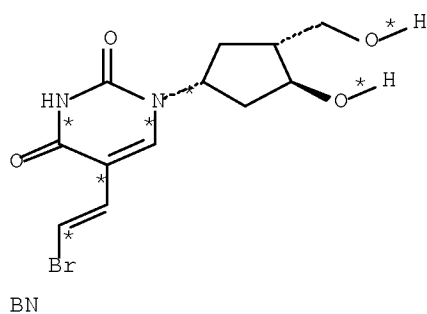
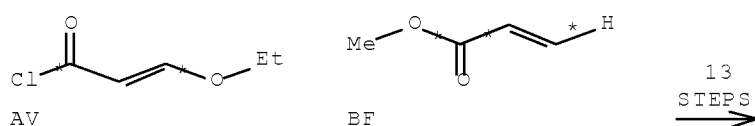
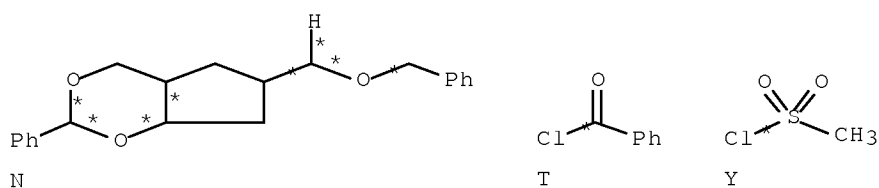


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RX(29) RCT BK 120963-48-6  
 RGT BO 298-14-6 KHCO<sub>3</sub>, BP 128-08-5 Bromosuccinimide  
 PRO BN 95463-56-2  
 SOL 68-12-2 DMF

RX(256) OF 267 COMPOSED OF RX(5), RX(7), RX(9), RX(11), RX(13), RX(15), RX(17),  
 RX(19), RX(21), RX(23), RX(25), RX(27), RX(29)

RX(256) N + T + Y + AV + BF ==> BN



RX(5) RCT N 120905-28-4  
 RGT Q 7664-93-9 H<sub>2</sub>SO<sub>4</sub>  
 PRO P 120236-98-8  
 SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4  
 RGT V 110-86-1 Pyridine  
 PRO U 120236-99-9  
 SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(9) RCT U 120236-99-9, Y 124-63-0

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RGT AA 121-44-8 Et3N  
PRO Z 116142-70-2  
SOL 75-09-2 CH2Cl2

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H2  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)  
RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)  
RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV ~~6191-99-7~~  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB ~~7553-56-2~~ I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

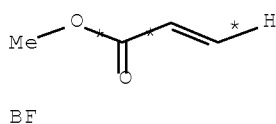
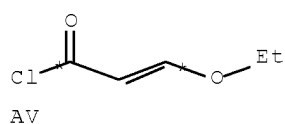
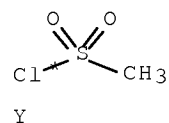
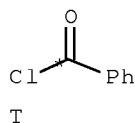
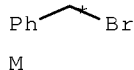
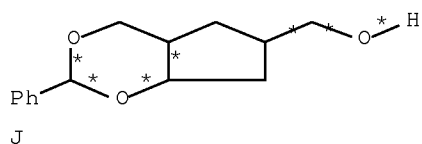
RX(27) RCT BG 120963-46-4  
RGT BL 1310-58-3 KOH  
PRO BK 120963-48-6

RX(29) RCT BK 120963-48-6  
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
PRO BN ~~95463-56-2~~  
SOL 68-12-2 DMF

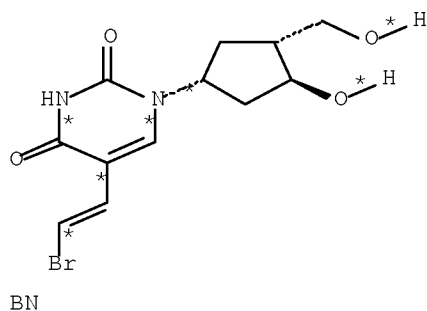
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RX(257) OF 267 COMPOSED OF RX(4), RX(5), RX(7), RX(9), RX(11), RX(13), RX(15),  
RX(17), RX(19), RX(21), RX(23), RX(25), RX(27), RX(29)

RX(257) J + M + T + Y + AV + BF ==>  
BN



14  
STEPS  
→



RX(4) RCT J 108275-94-1, M 100-39-0  
RGT O 7693-26-7 KH  
PRO N 120905-28-4  
SOL 109-99-9 THF

RX(5) RCT N 120905-28-4  
RGT Q 7664-93-9 H2SO4  
PRO P 120236-98-8  
SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO U 120236-99-9  
SOL 75-09-2 CH2Cl2

RX(9) RCT U 120236-99-9, Y 124-63-0  
RGT AA 121-44-8 Et3N

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PRO Z 116142-70-2  
SOL 75-09-2 CH2Cl2

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H2  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)  
RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)  
RGT AS 7664-41-7 NH3

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV ~~6191-99-7~~  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH2Cl2

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB ~~7553-56-2~~ I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

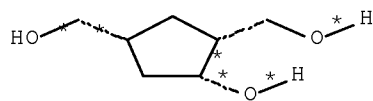
RX(27) RCT BG 120963-46-4  
RGT BL 1310-58-3 KOH  
PRO BK 120963-48-6

RX(29) RCT BK 120963-48-6  
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
PRO BN ~~95463-56-2~~  
SOL 68-12-2 DMF

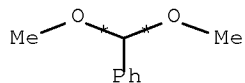
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RX(258) OF 267 COMPOSED OF RX(3), RX(4), RX(5), RX(7), RX(9), RX(11), RX(13),  
RX(15), RX(17), RX(19), RX(21), RX(23), RX(25), RX(27), RX(29)

RX(258) B + I + M + T + Y + AV + BF ==>  
BN



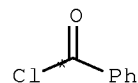
B



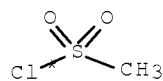
I



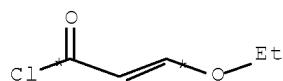
M



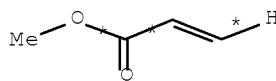
T



Y

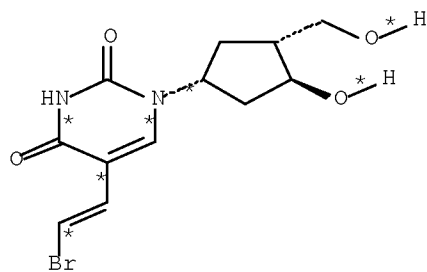


AV



BF

15  
STEPS  
→



BN

RX(3) RCT B 114129-19-0, I 1125-88-8  
RGT K 16872-11-0 HBF4  
PRO J 108275-94-1  
SOL 68-12-2 DMF

RX(4) RCT J 108275-94-1, M 100-39-0  
RGT O 7693-26-7 KH  
PRO N 120905-28-4  
SOL 109-99-9 THF

RX(5) RCT N 120905-28-4  
RGT Q 7664-93-9 H2SO4  
PRO P 120236-98-8  
SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO U 120236-99-9

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SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(9) RCT U 120236-99-9, Y 124-63-0  
RGT AA 121-44-8 Et<sub>3</sub>N  
PRO Z 116142-70-2  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H<sub>2</sub>  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)  
RGT AR 26386-88-9 (PhO)<sub>2</sub>P(O)N<sub>3</sub>  
SOL 71-43-2 Benzene

STAGE(2)  
RGT AS 7664-41-7 NH<sub>3</sub>

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(21) RCT AW 120905-35-3  
RGT AS 7664-41-7 NH<sub>3</sub>  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I<sub>2</sub>, BC 7697-37-2 HNO<sub>3</sub>  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh<sub>3</sub>, AA 121-44-8 Et<sub>3</sub>N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)<sub>2</sub>  
SOL 123-91-1 Dioxane

RX(27) RCT BG 120963-46-4  
RGT BL 1310-58-3 KOH  
PRO BK 120963-48-6

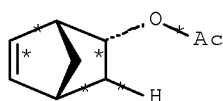
RX(29) RCT BK 120963-48-6

10/569486

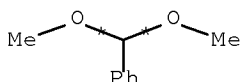
RGT BO 298-14-6 KHCO<sub>3</sub>, BP 128-08-5 Bromosuccinimide  
 PRO BN 95463-56-2  
 SOL 68-12-2 DMF

RX(259) OF 267 COMPOSED OF RX(1), RX(3), RX(4), RX(5), RX(7), RX(9), RX(11),  
 RX(13), RX(15), RX(17), RX(19), RX(21), RX(23), RX(25), RX(27),  
 RX(29)

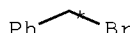
RX(259) A + I + M + T + Y + AV + BF ==>  
 BN



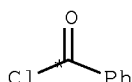
A



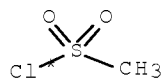
I



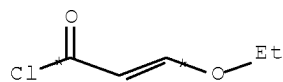
M



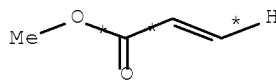
T



Y

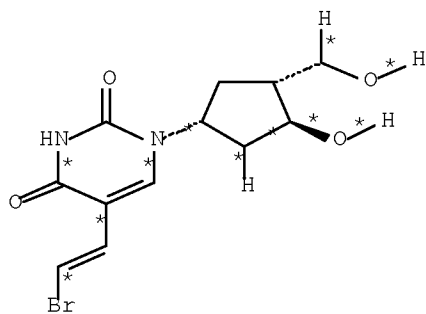


AV



BF

16  
 STEPS  
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BN

RX(1) RCT A 112836-09-6

STAGE(1)

RGT C 10028-15-6 Ozone  
 SOL 67-56-1 MeOH

STAGE(2)

RGT D 16853-85-3 LiAlH<sub>4</sub>  
 SOL 109-99-9 THF

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PRO B 114129-19-0

RX(3) RCT B 114129-19-0, I 1125-88-8  
RGT K ~~16872-11-0~~ HBF<sub>4</sub>  
PRO J 108275-94-1  
SOL 68-12-2 DMF

RX(4) RCT J 108275-94-1, M 100-39-0  
RGT O 7693-26-7 KH  
PRO N 120905-28-4  
SOL 109-99-9 THF

RX(5) RCT N 120905-28-4  
RGT Q 7664-93-9 H<sub>2</sub>SO<sub>4</sub>  
PRO P 120236-98-8  
SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4  
RGT V 110-86-1 Pyridine  
PRO U 120236-99-9  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(9) RCT U 120236-99-9, Y 124-63-0  
RGT AA 121-44-8 Et<sub>3</sub>N  
PRO Z 116142-70-2  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(11) RCT Z 116142-70-2  
RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
PRO AC 120905-29-5, AD 120905-30-8  
SOL 67-68-5 DMSO

RX(13) RCT AC 120905-29-5  
RGT AJ 1333-74-0 H<sub>2</sub>  
PRO AI 120905-32-0  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(15) RCT AI 120905-32-0  
RGT AO 20039-37-6 PDC  
PRO AN 120905-33-1  
SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

STAGE(1)  
RGT AR 26386-88-9 (PhO)<sub>2</sub>P(O)N<sub>3</sub>  
SOL 71-43-2 Benzene

STAGE(2)  
RGT AS 7664-41-7 NH<sub>3</sub>

PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AW 120905-35-3  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(21) RCT AW 120905-35-3



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RGT AS 7664-41-7 NH3  
PRO AY 120963-43-1  
SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BA 114179-59-8  
SOL 123-91-1 Dioxane

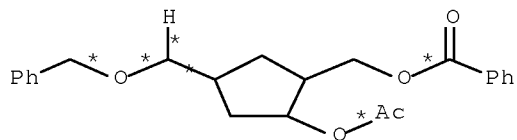
RX(25) RCT BA 114179-59-8, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BG 120963-46-4  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(27) RCT BG 120963-46-4  
RGT BL 1310-58-3 KOH  
PRO BK 120963-48-6

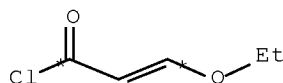
RX(29) RCT BK 120963-48-6  
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
PRO BN ~~95463-56-2~~  
SOL 68-12-2 DMF

RX(260) OF 267 COMPOSED OF RX(14), RX(16), RX(18), RX(20), RX(22), RX(24),  
RX(26), RX(28), RX(30)

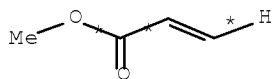
RX(260) AG + AV + BF ==> BQ



AG



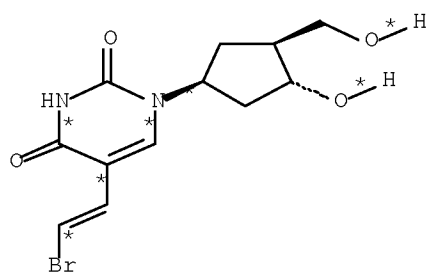
AV



BF

9  
STEPS  
→

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BQ

RX(14)	RCT	AG 120963-38-4
	RGT	AJ 1333-74-0 H2
	PRO	AM 120963-39-5
	CAT	7440-05-3 Pd
	SOL	64-17-5 EtOH
RX(16)	RCT	AM 120963-39-5
	RGT	AO 20039-37-6 PDC
	PRO	AP 120963-40-8
	SOL	68-12-2 DMF
RX(18)	RCT	AP 120963-40-8
	STAGE(1)	
	RGT	AR 26386-88-9 (PhO)2P(O)N3
	SOL	71-43-2 Benzene
	STAGE(2)	
	RGT	AS 7664-41-7 NH3
	PRO	AU 120963-41-9
RX(20)	RCT	AU 120963-41-9, AV 6191-99-7
	RGT	V 110-86-1 Pyridine
	PRO	AX 120963-42-0
	SOL	75-09-2 CH2Cl2
RX(22)	RCT	AX 120963-42-0
	RGT	AS 7664-41-7 NH3
	PRO	AZ 120963-44-2
	SOL	7732-18-5 Water
RX(24)	RCT	AZ 120963-44-2
	RGT	BB 7553-56-2 I2, BC 7697-37-2 HNO3
	PRO	BE 120963-45-3
	SOL	123-91-1 Dioxane
RX(26)	RCT	BE 120963-45-3, BF 96-33-3
	RGT	BH 603-35-0 PPh3, AA 121-44-8 Et3N
	PRO	BJ 120963-47-5
	CAT	3375-31-3 Pd(OAc)2
	SOL	123-91-1 Dioxane
RX(28)	RCT	BJ 120963-47-5

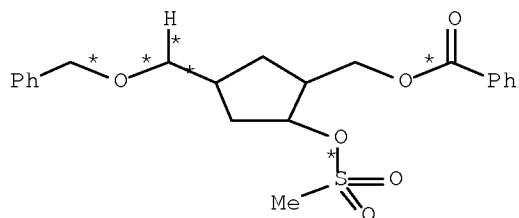
10/569486

RGT BL 1310-58-3 KOH  
PRO BM 120963-49-7

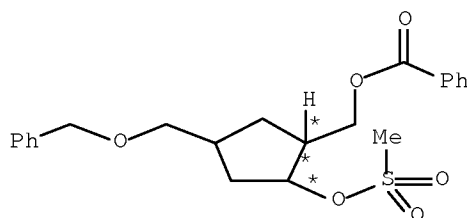
RX(30) RCT BM 120963-49-7  
RGT BO 298-14-6 KHCO<sub>3</sub>, BP 128-08-5 Bromosuccinimide  
PRO BQ 120963-50-0  
SOL 68-12-2 DMF

RX(261) OF 267 COMPOSED OF RX(12), RX(14), RX(16), RX(18), RX(20), RX(22),  
RX(24), RX(26), RX(28), RX(30)

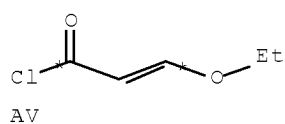
RX(261) 2 AB + AV + BF ==> BQ



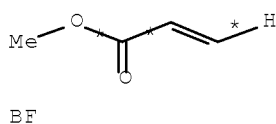
AB



AB

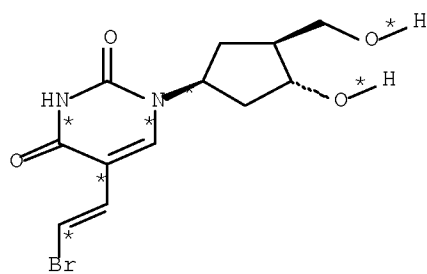


AV



BF

10  
STEPS  
→



BQ

RX(12) RCT AB 120963-37-3  
RGT AE 3396-11-0 Cs(OAc)<sub>2</sub>  
PRO AG 120963-38-4, AH 120905-31-9  
SOL 67-68-5 DMSO

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RX(14) RCT AG 120963-38-4  
RGT AJ 1333-74-0 H2  
PRO AM 120963-39-5  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
RGT AO 20039-37-6 PDC  
PRO AP 120963-40-8  
SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AX 120963-42-0  
SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
RGT AS 7664-41-7 NH3  
PRO AZ 120963-44-2  
SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BE 120963-45-3  
SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BJ 120963-47-5  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

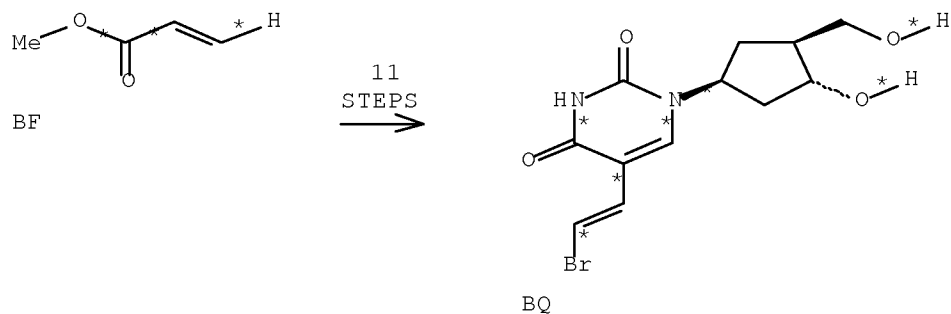
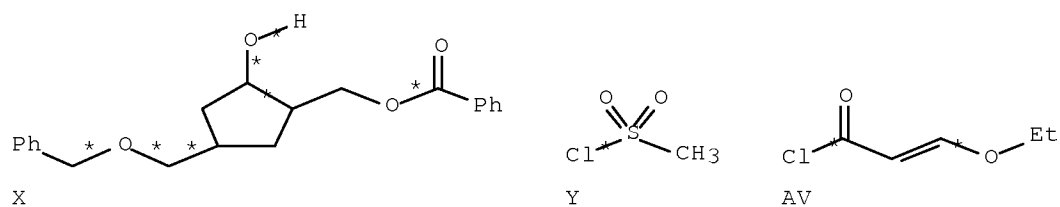
RX(28) RCT BJ 120963-47-5  
RGT BL 1310-58-3 KOH  
PRO BM 120963-49-7

RX(30) RCT BM 120963-49-7  
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
PRO BQ 120963-50-0  
SOL 68-12-2 DMF

RX(262) OF 267 COMPOSED OF RX(10), RX(12), RX(14), RX(16), RX(18), RX(20),  
RX(22), RX(24), RX(26), RX(28), RX(30)

RX(262) X + Y + AV + BF ==> BQ

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RX(10) RCT X 120963-36-2, Y 124-63-0  
 RGT AA 121-44-8 Et3N  
 PRO AB 120963-37-3  
 SOL 75-09-2 CH2Cl2

RX(12) RCT AB 120963-37-3  
 RGT AE 3396-11-0 Cs(OAc)2  
 PRO AG 120963-38-4, AH 120905-31-9  
 SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
 RGT AJ 1333-74-0 H2  
 PRO AM 120963-39-5  
 CAT 7440-05-3 Pd  
 SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
 RGT AO 20039-37-6 PDC  
 PRO AP 120963-40-8  
 SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)  
 RGT AR 26386-88-9 (PhO)2P(O)N3  
 SOL 71-43-2 Benzene

STAGE(2)  
 RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

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RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

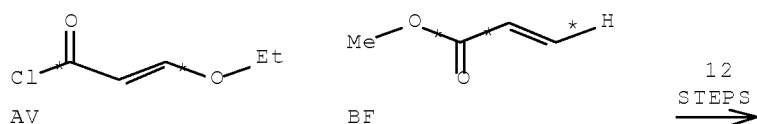
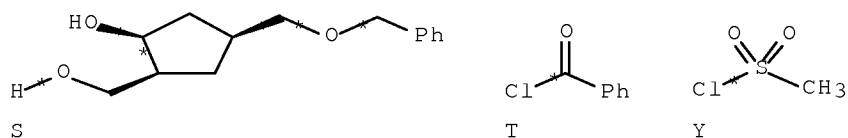
RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

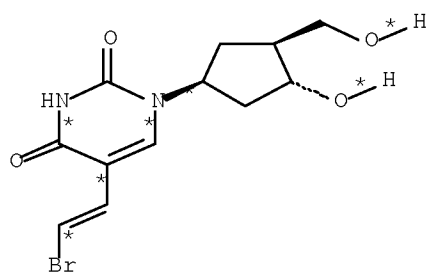
RX(30) RCT BM 120963-49-7  
 RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
 PRO BQ 120963-50-0  
 SOL 68-12-2 DMF

RX(263) OF 267 COMPOSED OF RX(8), RX(10), RX(12), RX(14), RX(16), RX(18),  
 RX(20), RX(22), RX(24), RX(26), RX(28), RX(30)

RX(263) S + T + Y + AV + BF ==> BQ



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BQ

RX(8) RCT S 120963-35-1, T 98-88-4  
 RGT V 110-86-1 Pyridine  
 PRO X 120963-36-2  
 SOL 75-09-2 CH2Cl2

RX(10) RCT X 120963-36-2, Y 124-63-0  
 RGT AA 121-44-8 Et3N  
 PRO AB 120963-37-3  
 SOL 75-09-2 CH2Cl2

RX(12) RCT AB 120963-37-3  
 RGT AE 3396-11-0 Cs(OAc)2  
 PRO AG 120963-38-4, AH 120905-31-9  
 SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
 RGT AJ 1333-74-0 H2  
 PRO AM 120963-39-5  
 CAT 7440-05-3 Pd  
 SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
 RGT AO 20039-37-6 PDC  
 PRO AP 120963-40-8  
 SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3  
 SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3

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PRO AZ 120963-44-2  
SOL 7732-18-5 Water

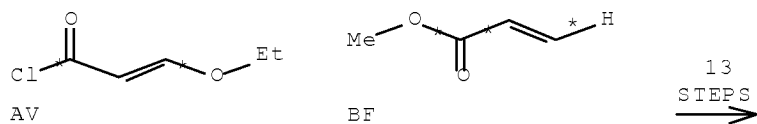
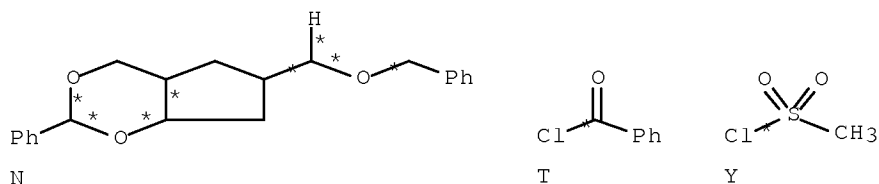
RX(24) RCT AZ 120963-44-2  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BE 120963-45-3  
SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BJ 120963-47-5  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
RGT BL 1310-58-3 KOH  
PRO BM 120963-49-7

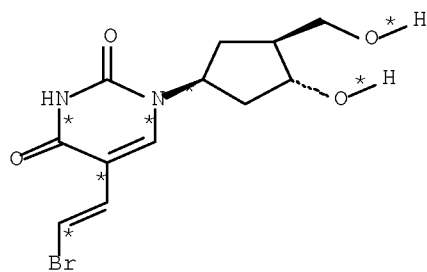
RX(30) RCT BM 120963-49-7  
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
PRO BQ 120963-50-0  
SOL 68-12-2 DMF

RX(264) OF 267 COMPOSED OF RX(6), RX(8), RX(10), RX(12), RX(14), RX(16),  
RX(18), RX(20), RX(22), RX(24), RX(26), RX(28), RX(30)  
RX(264) N + T + Y + AV + BF ==> BQ





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BQ

RX(6)	RCT	N 120905-28-4
	RGT	Q 7664-93-9 H2SO4
	PRO	S 120963-35-1
	SOL	7732-18-5 Water
RX(8)	RCT	S 120963-35-1, T 98-88-4
	RGT	V 110-86-1 Pyridine
	PRO	X 120963-36-2
	SOL	75-09-2 CH2Cl2
RX(10)	RCT	X 120963-36-2, Y 124-63-0
	RGT	AA 121-44-8 Et3N
	PRO	AB 120963-37-3
	SOL	75-09-2 CH2Cl2
RX(12)	RCT	AB 120963-37-3
	RGT	AE 3396-11-0 Cs(OAc)2
	PRO	AG 120963-38-4, AH 120905-31-9
	SOL	67-68-5 DMSO
RX(14)	RCT	AG 120963-38-4
	RGT	AJ 1333-74-0 H2
	PRO	AM 120963-39-5
	CAT	7440-05-3 Pd
	SOL	64-17-5 EtOH
RX(16)	RCT	AM 120963-39-5
	RGT	AO 20039-37-6 PDC
	PRO	AP 120963-40-8
	SOL	68-12-2 DMF
RX(18)	RCT	AP 120963-40-8
		STAGE(1)
		RGT AR 26386-88-9 (PhO)2P(O)N3
		SOL 71-43-2 Benzene
		STAGE(2)
		RGT AS 7664-41-7 NH3
		PRO AU 120963-41-9
RX(20)	RCT	AU 120963-41-9, AV 6191-99-7
	RGT	V 110-86-1 Pyridine

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PRO AX 120963-42-0  
SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
RGT AS 7664-41-7 NH3  
PRO AZ 120963-44-2  
SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BE 120963-45-3  
SOL 123-91-1 Dioxane

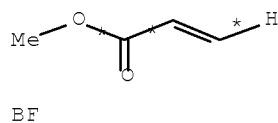
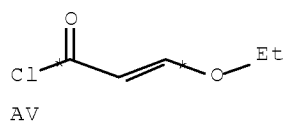
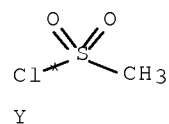
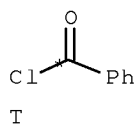
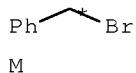
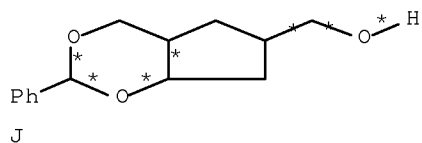
RX(26) RCT BE 120963-45-3, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BJ 120963-47-5  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
RGT BL 1310-58-3 KOH  
PRO BM 120963-49-7

RX(30) RCT BM 120963-49-7  
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
PRO BQ 120963-50-0  
SOL 68-12-2 DMF

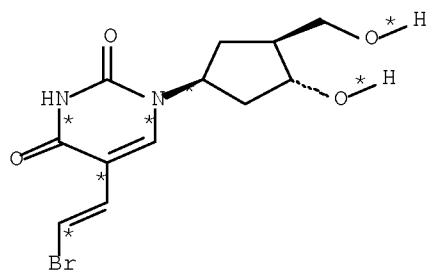
RX(265) OF 267 COMPOSED OF RX(4), RX(6), RX(8), RX(10), RX(12), RX(14), RX(16),  
RX(18), RX(20), RX(22), RX(24), RX(26), RX(28), RX(30)

RX(265) J + M + T + Y + AV + BF ==>  
EQ



14  
STEPS  
→

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BQ

RX(4) RCT J 108275-94-1, M 100-39-0  
 RGT O 7693-26-7 KH  
 PRO N 120905-28-4  
 SOL 109-99-9 THF

RX(6) RCT N 120905-28-4  
 RGT Q 7664-93-9 H2SO4  
 PRO S 120963-35-1  
 SOL 7732-18-5 Water

RX(8) RCT S 120963-35-1, T 98-88-4  
 RGT V 110-86-1 Pyridine  
 PRO X 120963-36-2  
 SOL 75-09-2 CH2Cl2

RX(10) RCT X 120963-36-2, Y 124-63-0  
 RGT AA 121-44-8 Et3N  
 PRO AB 120963-37-3  
 SOL 75-09-2 CH2Cl2

RX(12) RCT AB 120963-37-3  
 RGT AE 3396-11-0 Cs(OAc)2  
 PRO AG 120963-38-4, AH 120905-31-9  
 SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
 RGT AJ 1333-74-0 H2  
 PRO AM 120963-39-5  
 CAT 7440-05-3 Pd  
 SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
 RGT AO 20039-37-6 PDC  
 PRO AP 120963-40-8  
 SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)

RGT AR 26386-88-9 (PhO)2P(O)N3  
 SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

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PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
 RGT V 110-86-1 Pyridine  
 PRO AX 120963-42-0  
 SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
 RGT AS 7664-41-7 NH3  
 PRO AZ 120963-44-2  
 SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
 RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
 PRO BE 120963-45-3  
 SOL 123-91-1 Dioxane

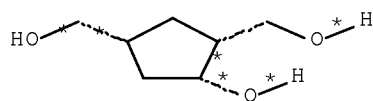
RX(26) RCT BE 120963-45-3, BF 96-33-3  
 RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
 PRO BJ 120963-47-5  
 CAT 3375-31-3 Pd(OAc)2  
 SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
 RGT BL 1310-58-3 KOH  
 PRO BM 120963-49-7

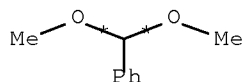
RX(30) RCT BM 120963-49-7  
 RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
 PRO BQ 120963-50-0  
 SOL 68-12-2 DMF

RX(266) OF 267 COMPOSED OF RX(3), RX(4), RX(6), RX(8), RX(10), RX(12), RX(14),  
 RX(16), RX(18), RX(20), RX(22), RX(24), RX(26), RX(28), RX(30)

RX(266) B + I + M + T + Y + AV + BF ==>  
 BQ



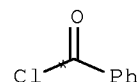
B



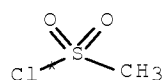
I



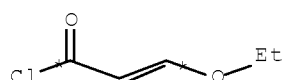
M



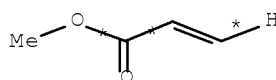
T



Y



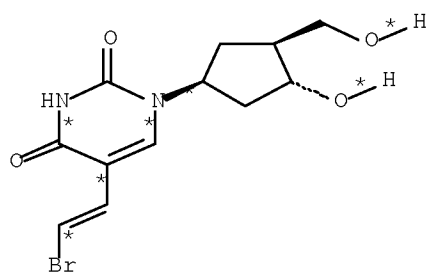
AV



BF

15  
STEPS  
→

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BQ

RX(3)	RCT	B 114129-19-0, I 1125-88-8
	RGT	K 16872-11-0 HBF <sub>4</sub>
	PRO	J 108275-94-1
	SOL	68-12-2 DMF
RX(4)	RCT	J 108275-94-1, M 100-39-0
	RGT	O 7693-26-7 KH
	PRO	N 120905-28-4
	SOL	109-99-9 THF
RX(6)	RCT	N 120905-28-4
	RGT	Q 7664-93-9 H <sub>2</sub> SO <sub>4</sub>
	PRO	S 120963-35-1
	SOL	7732-18-5 Water
RX(8)	RCT	S 120963-35-1, T 98-88-4
	RGT	V 110-86-1 Pyridine
	PRO	X 120963-36-2
	SOL	75-09-2 CH <sub>2</sub> Cl <sub>2</sub>
RX(10)	RCT	X 120963-36-2, Y 124-63-0
	RGT	AA 121-44-8 Et <sub>3</sub> N
	PRO	AB 120963-37-3
	SOL	75-09-2 CH <sub>2</sub> Cl <sub>2</sub>
RX(12)	RCT	AB 120963-37-3
	RGT	AE 3396-11-0 Cs(OAc) <sub>2</sub>
	PRO	AG 120963-38-4, AH 120905-31-9
	SOL	67-68-5 DMSO
RX(14)	RCT	AG 120963-38-4
	RGT	AJ 1333-74-0 H <sub>2</sub>
	PRO	AM 120963-39-5
	CAT	7440-05-3 Pd
	SOL	64-17-5 EtOH
RX(16)	RCT	AM 120963-39-5
	RGT	AO 20039-37-6 PDC
	PRO	AP 120963-40-8
	SOL	68-12-2 DMF
RX(18)	RCT	AP 120963-40-8

STAGE(1)

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RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)

RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AX 120963-42-0  
SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
RGT AS 7664-41-7 NH3  
PRO AZ 120963-44-2  
SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BE 120963-45-3  
SOL 123-91-1 Dioxane

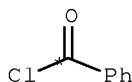
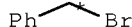
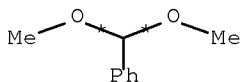
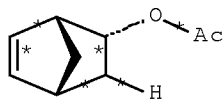
RX(26) RCT BE 120963-45-3, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BJ 120963-47-5  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
RGT BL 1310-58-3 KOH  
PRO BM 120963-49-7

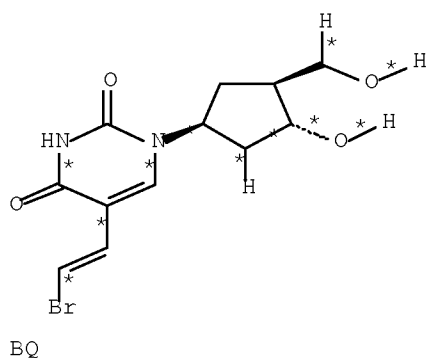
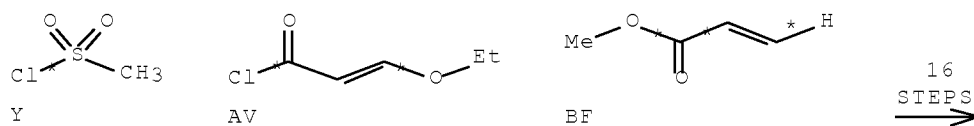
RX(30) RCT BM 120963-49-7  
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
PRO BQ 120963-50-0  
SOL 68-12-2 DMF

RX(267) OF 267 COMPOSED OF RX(1), RX(3), RX(4), RX(6), RX(8), RX(10), RX(12),  
RX(14), RX(16), RX(18), RX(20), RX(22), RX(24), RX(26), RX(28),  
RX(30)

RX(267) A + I + M + T + Y + AV + BF ==>  
EQ



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RX(1) RCT A 112836-09-6  
 STAGE(1)  
 RGT C 10028-15-6 Ozone  
 SOL 67-56-1 MeOH  
 STAGE(2)  
 RGT D 16853-85-3 LiAlH<sub>4</sub>  
 SOL 109-99-9 THF  
 PRO B 114129-19-0  
 RX(3) RCT B 114129-19-0, I 1125-88-8  
 RGT K 16872-11-0 HBF<sub>4</sub>  
 PRO J 108275-94-1  
 SOL 68-12-2 DMF  
 RX(4) RCT J 108275-94-1, M 100-39-0  
 RGT O 7693-26-7 KH  
 PRO N 120905-28-4  
 SOL 109-99-9 THF  
 RX(6) RCT N 120905-28-4  
 RGT Q 7664-93-9 H<sub>2</sub>SO<sub>4</sub>  
 PRO S 120963-35-1  
 SOL 7732-18-5 Water  
 RX(8) RCT S 120963-35-1, T 98-88-4  
 RGT V 110-86-1 Pyridine  
 PRO X 120963-36-2  
 SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

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RX(10) RCT X 120963-36-2, Y 124-63-0  
RGT AA 121-44-8 Et3N  
PRO AB 120963-37-3  
SOL 75-09-2 CH2Cl2

RX(12) RCT AB 120963-37-3  
RGT AE 3396-11-0 Cs(OAc)2  
PRO AG 120963-38-4, AH 120905-31-9  
SOL 67-68-5 DMSO

RX(14) RCT AG 120963-38-4  
RGT AJ 1333-74-0 H2  
PRO AM 120963-39-5  
CAT 7440-05-3 Pd  
SOL 64-17-5 EtOH

RX(16) RCT AM 120963-39-5  
RGT AO 20039-37-6 PDC  
PRO AP 120963-40-8  
SOL 68-12-2 DMF

RX(18) RCT AP 120963-40-8

STAGE(1)  
RGT AR 26386-88-9 (PhO)2P(O)N3  
SOL 71-43-2 Benzene

STAGE(2)  
RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7  
RGT V 110-86-1 Pyridine  
PRO AX 120963-42-0  
SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0  
RGT AS 7664-41-7 NH3  
PRO AZ 120963-44-2  
SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2  
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3  
PRO BE 120963-45-3  
SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3  
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N  
PRO BJ 120963-47-5  
CAT 3375-31-3 Pd(OAc)2  
SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5  
RGT BL 1310-58-3 KOH  
PRO BM 120963-49-7

RX(30) RCT BM 120963-49-7  
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide  
PRO BQ 120963-50-0



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SOL 68-12-2 DMF

L46 ANSWER 18 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 107:40117 CASREACT Full-text

TITLE: Stereoselective synthesis of (±)-cis- $\alpha$ -irone

AUTHOR(S): Nussbaumer, Cornelius; Frater, Georg

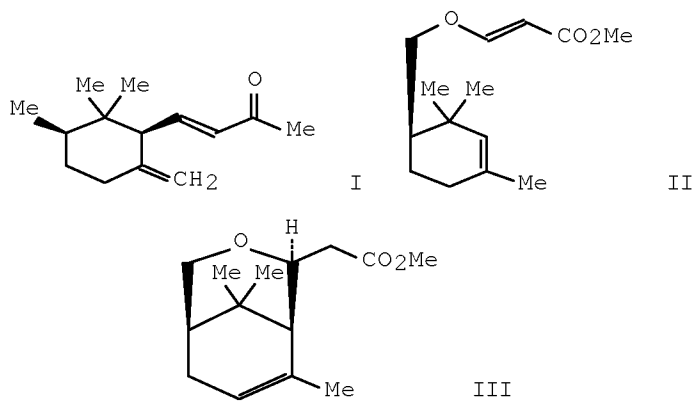
CORPORATE SOURCE: Givaudan Forschungsges. A.-G., Duebendorf, CH-8600, Switz.

SOURCE: Journal of Organic Chemistry (1987), 52(10), 2096-8  
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: English

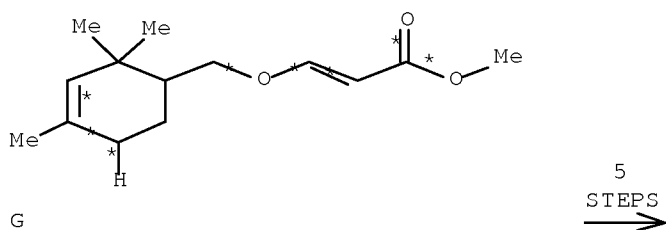
GI



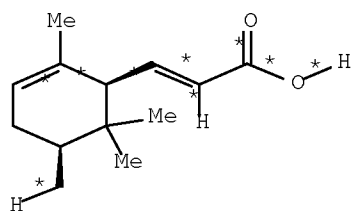
AB (±)-cis-Irone (I) was stereoselectively synthesized in 36% overall yield in 7 steps from (2,2,4-trimethyl-3-cyclohexen-1-yl)methanol via a  $\beta$ -alkoxyacrylate-olefin cyclization of II to III as the key step.

RX(24) OF 28 COMPOSED OF RX(3), RX(4), RX(5), RX(6), RX(7)

RX(24) G ==> A



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A  
YIELD 76%

RX(3) RCT G 107890-58-4  
RGT K 67-56-1 MeOH  
PRO J 107890-60-8  
SOL 75-09-2 CH2Cl2

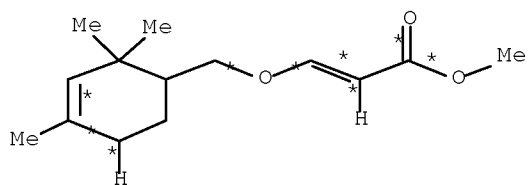
RX(4) RCT J 107890-60-8  
RGT N 1310-73-2 NaOH  
PRO M 107890-61-9  
SOL 67-56-1 MeOH, 7732-18-5 Water

RX(5) RCT M 107890-61-9  
RGT Q 4111-54-0 LiN(Pr-i)2  
PRO P 107890-62-0  
SOL 109-99-9 THF, 110-54-3 Hexane

RX(6) RCT P 107890-62-0  
RGT U 124-63-0 MeSO2Cl  
PRO T 107890-63-1  
SOL 75-09-2 CH2Cl2, 110-86-1 Pyridine

RX(7) RCT T 107890-63-1  
RGT W 7631-82-5 NaI, X 7440-66-6 Zn  
PRO A 107890-64-2  
SOL 110-71-4 (CH2OMe)2

RX(27) OF 28 COMPOSED OF RX(3), RX(4), RX(5), RX(6), RX(7), RX(1)  
RX(27) G + B ==> C



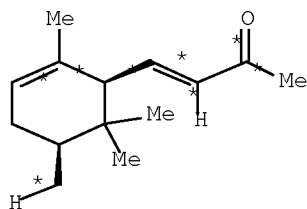
G

H3C-Li

B

6  
STEPS  
→

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C  
YIELD 89%

RX(3) RCT G 107890-58-4  
RGT K 67-56-1 MeOH  
PRO J 107890-60-8  
SOL 75-09-2 CH2Cl2

RX(4) RCT J 107890-60-8  
RGT N 1310-73-2 NaOH  
PRO M 107890-61-9  
SOL 67-56-1 MeOH, 7732-18-5 Water

RX(5) RCT M 107890-61-9  
RGT Q 4111-54-0 LiN(Pr-i)2  
PRO P 107890-62-0  
SOL 109-99-9 THF, 110-54-3 Hexane

RX(6) RCT P 107890-62-0  
RGT U 124-63-0 MeSO2Cl  
PRO T 107890-63-1  
SOL 75-09-2 CH2Cl2, 110-86-1 Pyridine

RX(7) RCT T 107890-63-1  
RGT W 7681-82-5 NaI, X 7440-66-6 Zn  
PRO A 107890-64-2  
SOL 110-71-4 (CH2OMe)2

RX(1) RCT A 107890-64-2, B 917-54-4  
PRO C 472-46-8  
SOL 60-29-7 Et2O

L46 ANSWER 19 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 99:53063 CASREACT Full-text  
TITLE: 3-Alkoxyacroleins: malonic dialdehyde equivalents  
AUTHOR(S): Maddaluno, Jacques; D'Angelo, Jean  
CORPORATE SOURCE: Lab. Chim. Org. Synth., Univ. Pierre et Marie Curie,  
Paris, 75005, Fr.  
SOURCE: Tetrahedron Letters (1983), 24(9), 895-8  
CODEN: TELEAY; ISSN: 0040-4039  
DOCUMENT TYPE: Journal  
LANGUAGE: French

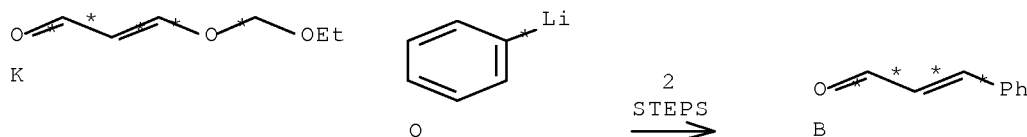
AB (E)-ROCH:CHCHO (I; R = Me, MeOCH2, EtOCH2, PhCH2OCH2), useful as synthetic  
equivs. of malondialdehyde, were prepared in 80% yield by alkylation of  
NaOCH:CHCHO with MeO3SF, MeOCH2Cl, EtOCH2Cl, and PhCH2OCH2Cl, resp., at room  
temperature for 12 h. Some synthetic applications of I are described. E.g.,  
treatment of I with organolithiums gave  $\alpha$ -substituted allylic alcs. which were

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hydrolyzed by acids to give  $\beta$ -substituted acroleins. Thus, I (R = EtOCH<sub>2</sub>) with PhLi cong. NH<sub>4</sub>Cl at -78° for 10 min gave (E)-EtOCH<sub>2</sub>OCH:CHCHPhOH which was hydrolyzed by acid to give HCOCH:CHPh.

RX(15) OF 18 COMPOSED OF RX(7), RX(1)

RX(15) K + O ==> E



RX(7) RCT K 86557-99-5, O 591-51-5  
PRO A 86558-09-0

RX(1) RCT A 86558-09-0  
RGT C 7647-01-0 HCl  
PRO B 104-55-2

L46 ANSWER 20 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 95:203164 CASREACT [Full-text](#)

TITLE: Rearrangement of N-acetylacetaldehyde derivatives of indoles. Part 5. Di- and tetrahydro derivatives of rearrangement products of 4-(tetrahydrocarbazol-9-yl)-3-buten-2-one

AUTHOR(S): Teuber, Hans Joachim; Gholami, Abbas; Reinehr, Ulrich; Paulus, Erich

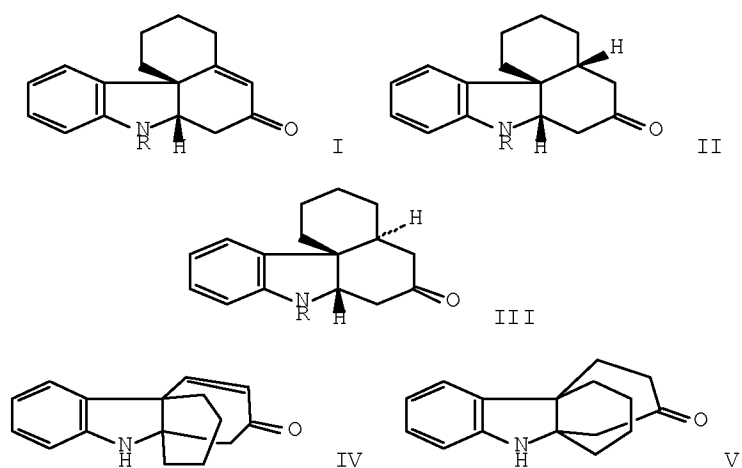
CORPORATE SOURCE: Inst. Org. Chem., Univ. Frankfurt, Frankfurt/Main, D-6000/50, Fed. Rep. Ger.

SOURCE: Liebigs Annalen der Chemie (1981), (4), 569-80  
CODEN: LACHDL; ISSN: 0170-2041

DOCUMENT TYPE: Journal

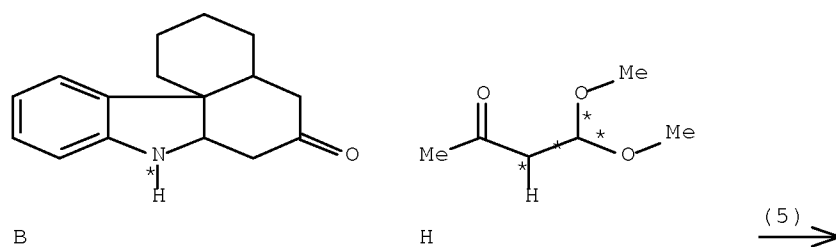
LANGUAGE: German

GI

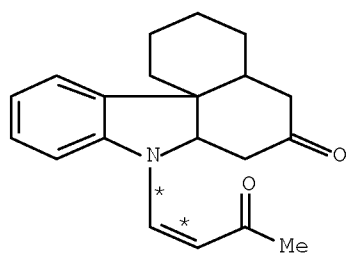


AB    Catalytic hydrogenation of I (R = H, CH:CHCOMe) gave II and III (same R), the configurations of which were assigned by x-ray anal. The relative configurations of the chiral centers in III (R = H) were determined, and the cyclohexanone ring was shown to have the boat conformation. NaBH<sub>4</sub> reduction of I (R = H) and III occurred stereoselectively to give the corresponding alcs. with axial and equatorial OH groups, resp. Both the configuration and the conformation of these alcs. could be determined from IR and NMR spectra. NaBH<sub>4</sub> reduction of II (R = H), IV, and V gave epimeric mixts. of alcs.

RX(5) OF 12            ...B + H ==> G



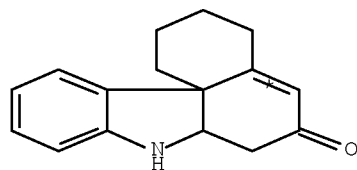
10/569486



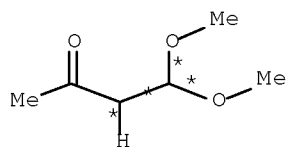
G  
YIELD 54%

RX(5) RCT B 72181-49-8, H 5436-21-5  
RGT I 7647-01-0 HCl  
PRO G 72181-58-9

RX(10) OF 12 COMPOSED OF RX(1), RX(5)  
RX(10) A + H ==> G

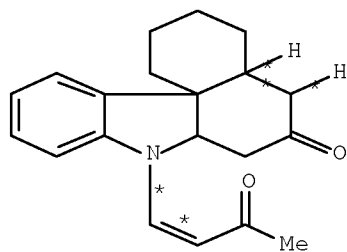


A



H

2  
STEPS  
→



G  
YIELD 54%

RX(1) RCT A 2398-19-8  
PRO B 72181-49-8  
CAT 7727-43-7 BaSO4

RX(5) RCT B 72181-49-8, H 5436-21-5  
RGT I 7647-01-0 HCl

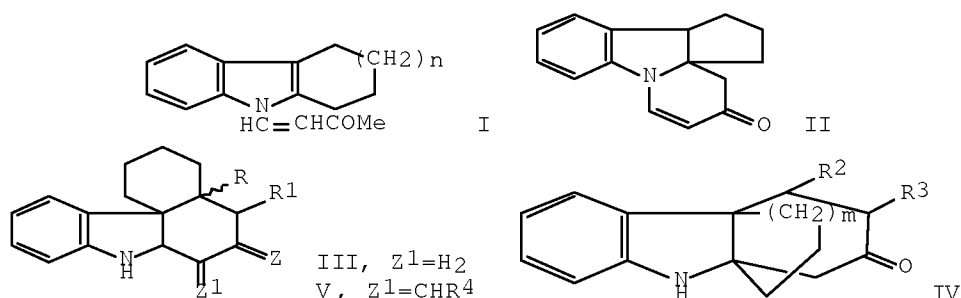
L46 ANSWER 21 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 92:58534 CASREACT Full-textTITLE: Rearrangement of 4-(tetrahydrocarbazol-9-yl)- and  
4-(tetrahydrocyclopent[b]indol-4-yl)-3-buten-2-oneAUTHOR(S): Teuber, Hans Joachim; Gholami, Abbas; Reinehr, Ulrich;  
Bader, Hans JoachimCORPORATE SOURCE: Inst. Org. Chem., Univ. Frankfurt, Frankfurt/Main,  
D-6000/50, Fed. Rep. Ger.SOURCE: Liebigs Annalen der Chemie (1979), (7), 1048-66  
CODEN: LACHDL; ISSN: 0170-2041

DOCUMENT TYPE: Journal

LANGUAGE: German

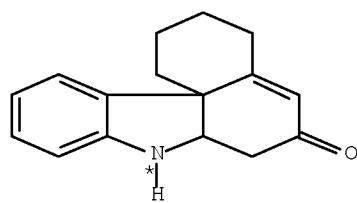
GI



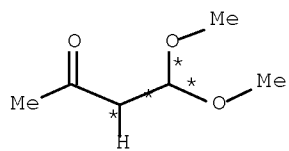
AB Cycloalkanoindoles I ( $n = 0, 1$ ) reacted in HCl-MeOH to give, besides the cyclization product II, the rearrangement products ketones III ( $RR1 = \text{bond}, Z = O$ ) and IV ( $R2R3 = \text{bond}, m = 1, 2$ ) with propellane structure. II and IV ( $R2R3 = \text{bond}, m = 2$ ) as well as IV ( $R2R3 = \text{bond}, m = 1$ ) and III ( $RR1 = \text{bond}, Z = O$ ) are in equilibrium III ( $RR1 = \text{bond}, Z = O$ ) was hydrogenated to III ( $R = R1 = H, Z = O$ ), which was isolated in 2 stereoisomeric forms corresponding to cis- and trans-decalone. The N-benzoyl derivative of II ( $R = R1 = H, Z = H2$ ), formed by hydrogenation, has the same structure as the appropriately modified product obtained by Fischer cyclization from trans- $\alpha$ -decalone. III ( $RR1 = \text{bond}, Z = O$ ) and IV ( $R2R3 = \text{bond}, m = 1, 2$ ), as well as the corresponding saturated ketones III ( $R = R1 = H, Z = O$ ) and IV ( $R2 = R3 = H, m = 1, 2$ ) were converted into derivs. by reaction at the oxo and amino functions. III ( $RR1 = \text{bond}, Z = O$ ) and BzH with Na-EtOH gave the benzylidene derivative V ( $RR1 = \text{bond}, R4 = Ph$ ).

RX(4) OF 67 ...E + I ==&gt; J...

10/569486

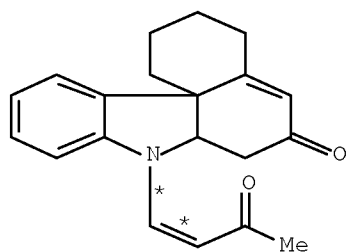


E



I

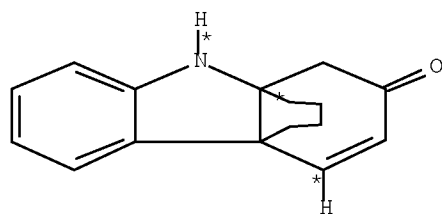
(4)  $\longrightarrow$



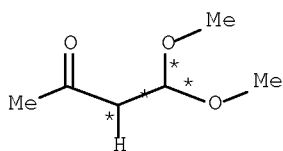
J  
YIELD 63%

RX(4)      RCT   E 2398-19-8, I 5436-21-5  
              RGT   F 7647-01-0 HCl  
              PRO   J 2398-25-6

RX(5) OF 67      ...E + I ==> J...



H

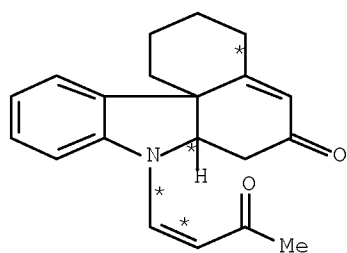


I

(5)  $\longrightarrow$



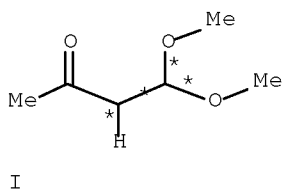
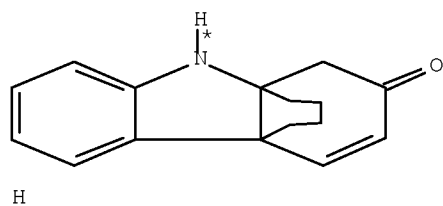
10/569486



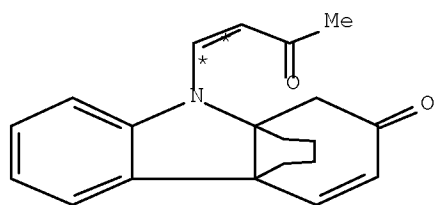
J  
YIELD 78%

RX(5)      RCT   H 69393-74-4, I 5436-21-5  
             RGT   F 7647-01-0 HCl  
             PRO   J 2398-25-6

RX(17) OF 67      ...H + I ==> AF



(17)  
→

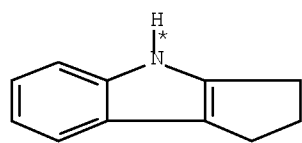


AF  
YIELD 54%

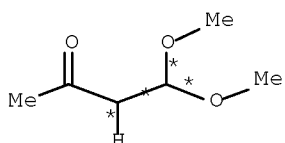
RX(17)      RCT   H 69393-74-4, I 5436-21-5  
             RGT   F 7647-01-0 HCl  
             PRO   AF 72181-69-2

RX(22) OF 67      ...B + I ==> K...

10/569486

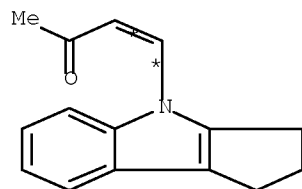


B



I

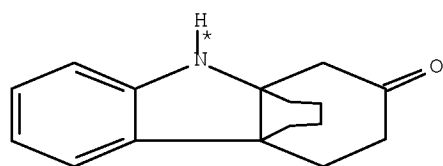
(22)



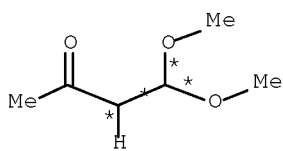
K  
YIELD 40%

RX(22)      RCT   B 2047-91-8, I 5436-21-5  
                  RGT   F 7647-01-0 HCl  
                  PRO   K 69393-75-5

RX(25) OF 67      ...AG + I ==> AN

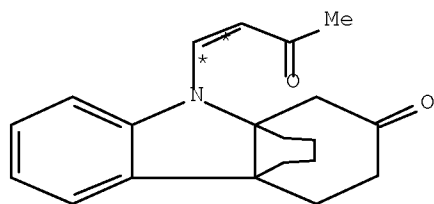


AG



I

(25)

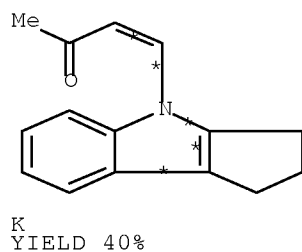
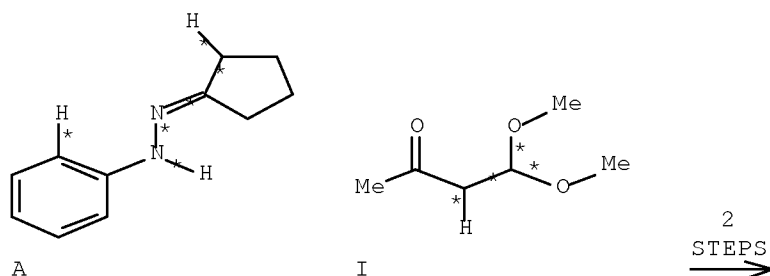


AN  
YIELD 63%

10/569486

RX(25) RCT AG 72181-70-5, I 5436-21-5  
RGT F 7647-01-0 HCl  
PRO AN 72181-73-8

RX(26) OF 67 COMPOSED OF RX(1), RX(22)  
RX(26) A + I ==> K

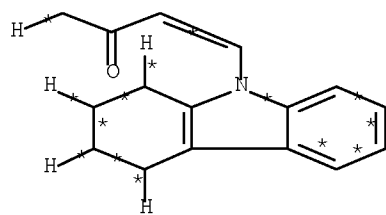


RX(1) RCT A 1132-58-7  
RGT C 7664-93-9 H2SO4  
PRO B 2047-91-8

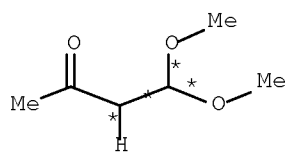
RX(22) RCT B 2047-91-8, I 5436-21-5  
RGT F 7647-01-0 HCl  
PRO K 69393-75-5

RX(28) OF 67 COMPOSED OF RX(2), RX(4)  
RX(28) D + I ==> J

10/569486

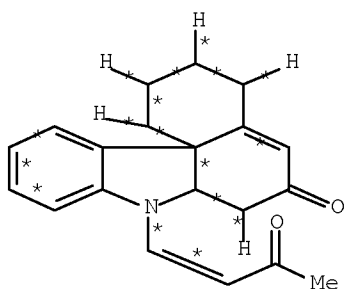


D



I

2  
STEPS  
→

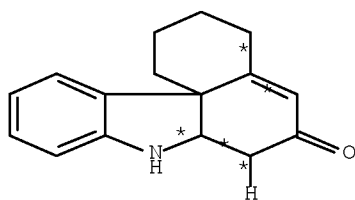


J  
YIELD 63%

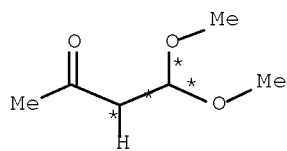
RX(2)      RCT   D 2646-01-7  
             RGT   F 7647-01-0 HCl  
             PRO   E 2398-19-8  
             SOL   67-56-1 MeOH

RX(4)      RCT   E 2398-19-8, I 5436-21-5  
             RGT   F 7647-01-0 HCl  
             PRO   J 2398-25-6

RX(36) OF 67 COMPOSED OF RX(3), RX(5)  
RX(36)      E + I ==> J



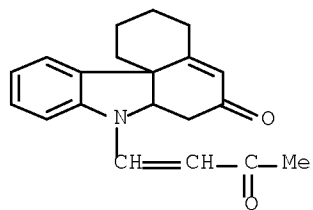
E



I

2  
STEPS  
→

10/569486



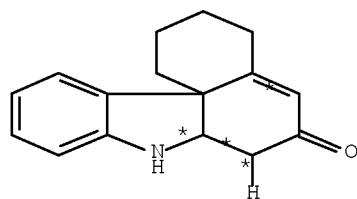
J  
YIELD 78%

RX(3)      RCT   E 2398-19-8  
              RGT   F 7647-01-0 HCl  
              PRO   H 69393-74-4  
              SOL   67-56-1 MeOH

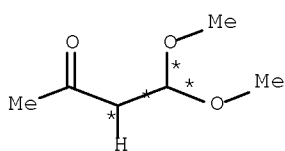
RX(5)      RCT   H 69393-74-4, I 5436-21-5  
              RGT   F 7647-01-0 HCl  
              PRO   J 2398-25-6

RX(37) OF 67 COMPOSED OF RX(3), RX(17)

RX(37)      E   +   I   ==>   AF

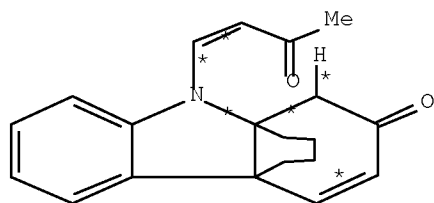


E



I

2  
STEPS  
→



AF  
YIELD 54%

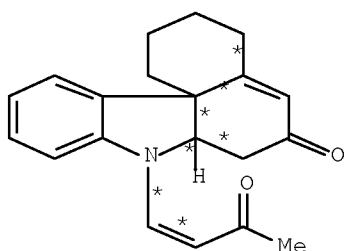
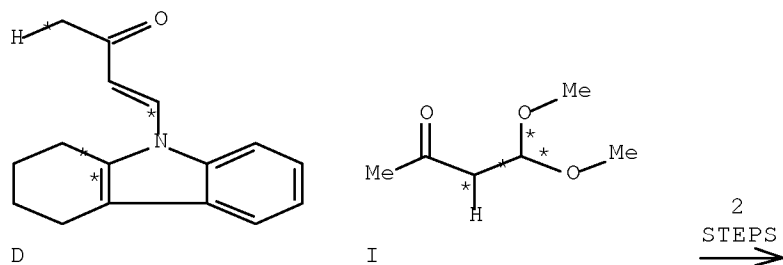
RX(3)      RCT   E 2398-19-8

10/569486

RGT F 7647-01-0 HCl  
PRO H 69393-74-4  
SOL 67-56-1 MeOH

RX(17) RCT H 69393-74-4, I 5436-21-5  
RGT F 7647-01-0 HCl  
PRO AF 72181-69-2

RX(39) OF 67 COMPOSED OF RX(21), RX(5)  
RX(39) D + I ==> J



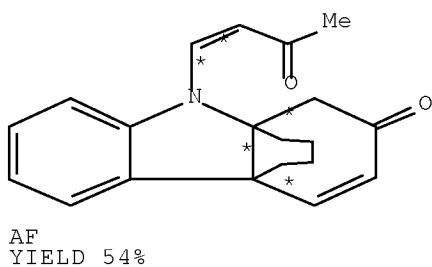
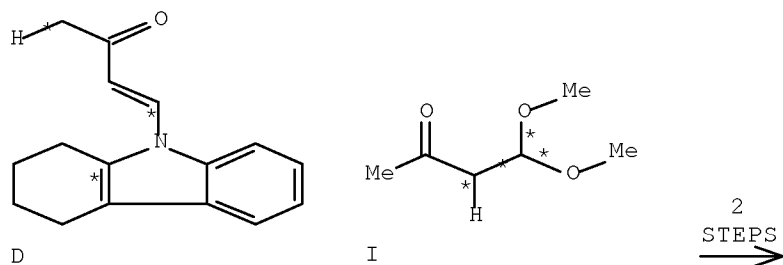
J  
YIELD 78%

RX(21) RCT D 2646-01-7  
RGT F 7647-01-0 HCl  
PRO H 69393-74-4  
SOL 67-56-1 MeOH

RX(5) RCT H 69393-74-4, I 5436-21-5  
RGT F 7647-01-0 HCl  
PRO J 2398-25-6

RX(40) OF 67 COMPOSED OF RX(21), RX(17)  
RX(40) D + I ==> AF

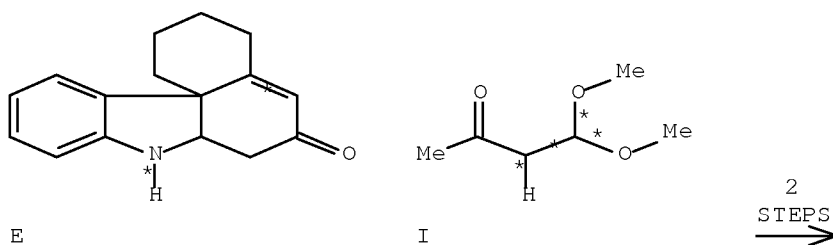
10/569486



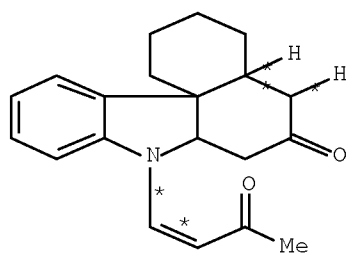
RX(21) RCT D 2646-01-7  
RGT F 7647-01-0 HCl  
PRO H 69393-74-4  
SOL 67-56-1 MeOH

RX(17) RCT H 69393-74-4, I 5436-21-5  
RGT F 7647-01-0 HCl  
PRO AF 72181-69-2

RX(42) OF 67 COMPOSED OF RX(4), RX(12)  
RX(42) E + I ==> Y



10/569486



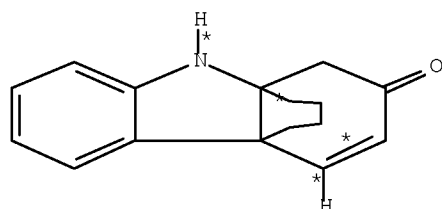
Y  
YIELD 47%

RX(4) RCT E 2398-19-8, I 5436-21-5  
RGT F 7647-01-0 HCl  
PRO J 2398-25-6

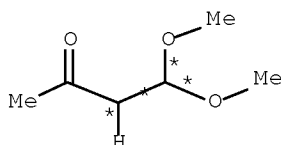
RX(12) RCT J 2398-25-6  
RGT X 7727-43-7 BaSO4  
PRO Y 72181-58-9

RX(43) OF 67 COMPOSED OF RX(5), RX(12)

RX(43) H + I ==> Y

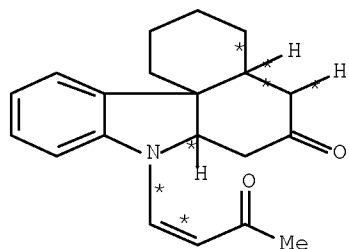


H



I

2  
STEPS  
→



Y  
YIELD 47%

RX(5) RCT H 69393-74-4, I 5436-21-5  
RGT F 7647-01-0 HCl



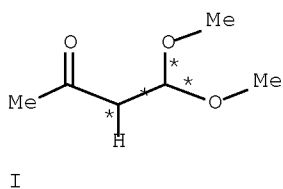
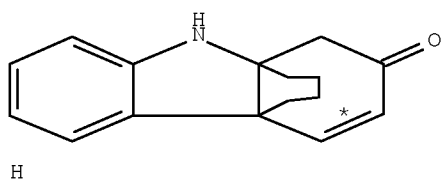
10/569486

PRO J 2398-25-6

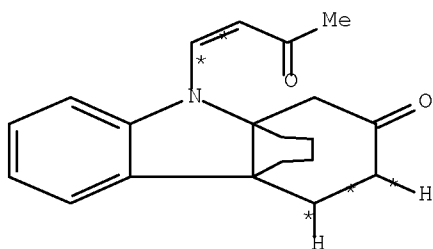
RX(12) RCT J 2398-25-6  
RGT X 7727-43-7 BaSO4  
PRO Y 72181-58-9

RX(48) OF 67 COMPOSED OF RX(18), RX(25)

RX(48) H + I ==> AN



2  
STEPS  
→



YIELD 63%

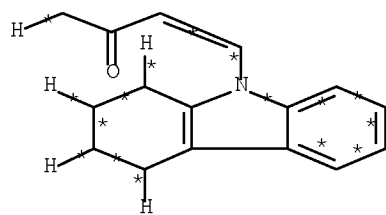
RX(18) RCT H 69393-74-4  
RGT X 7727-43-7 BaSO4  
PRO AG 72181-70-5

RX(25) RCT AG 72181-70-5, I 5436-21-5  
RGT F 7647-01-0 HCl  
PRO AN 72181-73-8

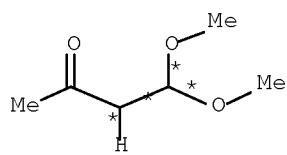
RX(53) OF 67 COMPOSED OF RX(2), RX(3), RX(5)

RX(53) D + I ==> J

10/569486

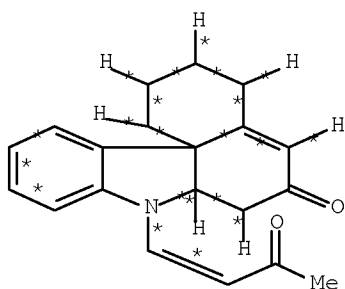


D



I

3  
STEPS  
→



J  
YIELD 78%

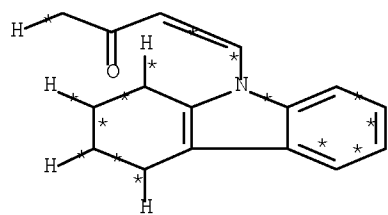
RX(2)      RCT   D 2646-01-7  
             RGT   F 7647-01-0 HCl  
             PRO   E 2398-19-8  
             SOL   67-56-1 MeOH

RX(3)      RCT   E 2398-19-8  
             RGT   F 7647-01-0 HCl  
             PRO   H 69393-74-4  
             SOL   67-56-1 MeOH

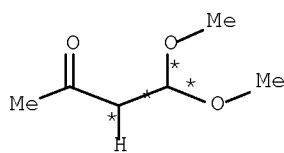
RX(5)      RCT   H 69393-74-4, I 5436-21-5  
             RGT   F 7647-01-0 HCl  
             PRO   J 2398-25-6

RX(54) OF 67 COMPOSED OF RX(2), RX(3), RX(17)  
RX(54)      D + I ==> AF

10/569486

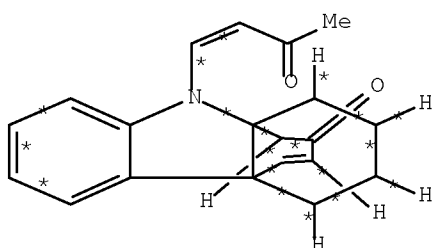


D



I

3  
STEPS  
➔



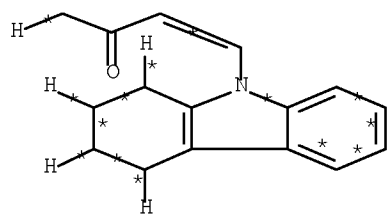
AF  
YIELD 54%

RX(2)      RCT    D 2646-01-7  
             RGT    F 7647-01-0 HCl  
             PRO    E 2398-19-8  
             SOL    67-56-1 MeOH

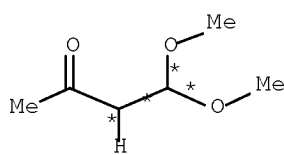
RX(3)      RCT    E 2398-19-8  
             RGT    F 7647-01-0 HCl  
             PRO    H 69393-74-4  
             SOL    67-56-1 MeOH

RX(17)     RCT    H 69393-74-4, I 5436-21-5  
             RGT    F 7647-01-0 HCl  
             PRO    AF 72181-69-2

RX(56) OF 67 COMPOSED OF RX(2), RX(4), RX(12)  
RX(56)      D + I ==> Y



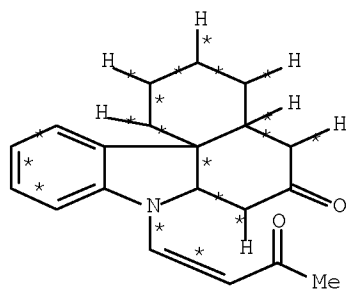
D



I

3  
STEPS  
➔

10/569486



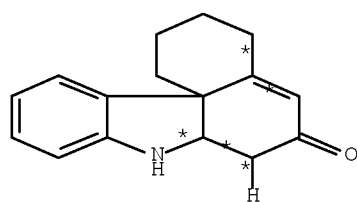
Y  
YIELD 47%

RX(2) RCT D 2646-01-7  
RGT F 7647-01-0 HCl  
PRO E 2398-19-8  
SOL 67-56-1 MeOH

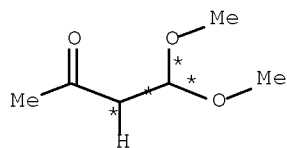
RX(4) RCT E 2398-19-8, I 5436-21-5  
RGT F 7647-01-0 HCl  
PRO J 2398-25-6

RX(12) RCT J 2398-25-6  
RGT X 7727-43-7 BaSO4  
PRO Y 72181-58-9

RX(60) OF 67 COMPOSED OF RX(3), RX(5), RX(12)  
RX(60) E + I ==> Y



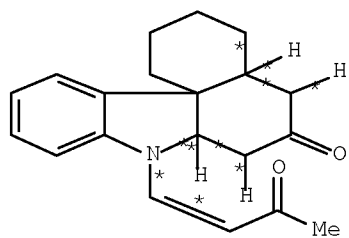
E



I

3  
STEPS  
→

10/569486



Y  
YIELD 47%

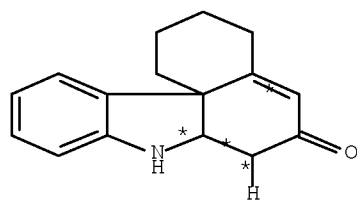
RX(3)      RCT   E 2398-19-8  
             RGT   F 7647-01-0 HCl  
             PRO   H 69393-74-4  
             SOL   67-56-1 MeOH

RX(5)      RCT   H 69393-74-4, I 5436-21-5  
             RGT   F 7647-01-0 HCl  
             PRO   J 2398-25-6

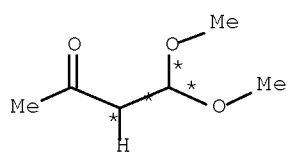
RX(12)     RCT   J 2398-25-6  
             RGT   X 7727-43-7 BaSO4  
             PRO   Y 72181-58-9

RX(61) OF 67 COMPOSED OF RX(3), RX(18), RX(25)

RX(61)      E   +   I   ==>   AN

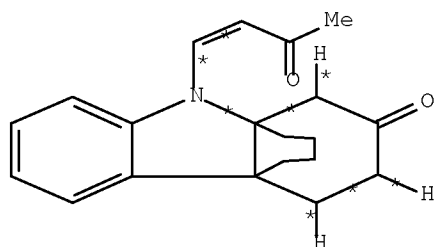


E



I

3  
STEPS  
→



AN  
YIELD 63%

10/569486

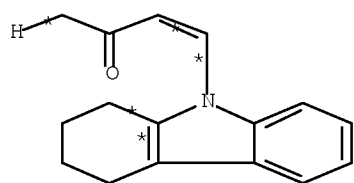
RX(3) RCT E 2398-19-8  
RGT F 7647-01-0 HCl  
PRO H 69393-74-4  
SOL 67-56-1 MeOH

RX(18) RCT H 69393-74-4  
RGT X 7727-43-7 BaSO4  
PRO AG 72181-70-5

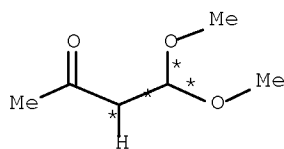
RX(25) RCT AG 72181-70-5, I 5436-21-5  
RGT F 7647-01-0 HCl  
PRO AN 72181-73-8

RX(62) OF 67 COMPOSED OF RX(21), RX(5), RX(12)

RX(62) D + I ==> Y

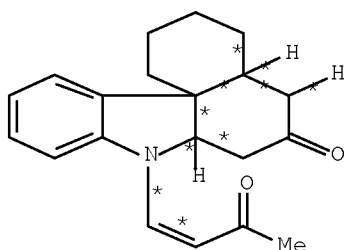


D



I

3  
STEPS  
→



Y  
YIELD 47%

RX(21) RCT D 2646-01-7  
RGT F 7647-01-0 HCl  
PRO H 69393-74-4  
SOL 67-56-1 MeOH

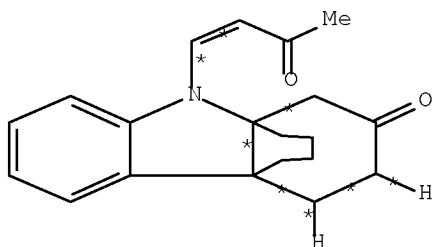
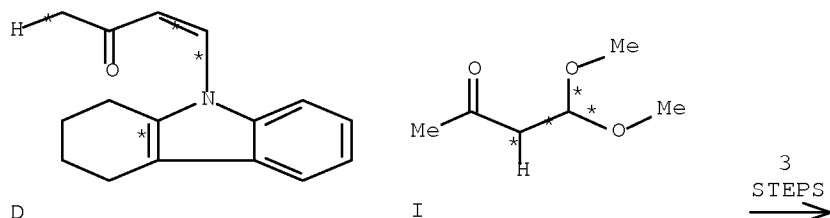
RX(5) RCT H 69393-74-4, I 5436-21-5  
RGT F 7647-01-0 HCl  
PRO J 2398-25-6

RX(12) RCT J 2398-25-6

10/569486

RGT X 7727-43-7 BaSO4  
PRO Y 72181-58-9

RX(63) OF 67 COMPOSED OF RX(21), RX(18), RX(25)  
RX(63) D + I ==> AN



AN  
YIELD 63%

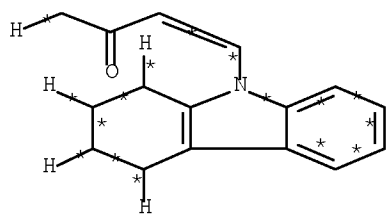
RX(21) RCT D 2646-01-7  
RGT F 7647-01-0 HCl  
PRO H 69393-74-4  
SOL 67-56-1 MeOH

RX(18) RCT H 69393-74-4  
RGT X 7727-43-7 BaSO4  
PRO AG 72181-70-5

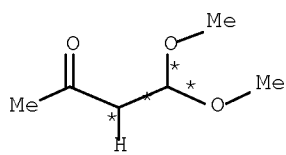
RX(25) RCT AG 72181-70-5, I 5436-21-5  
RGT F 7647-01-0 HCl  
PRO AN 72181-73-8

RX(64) OF 67 COMPOSED OF RX(2), RX(3), RX(5), RX(12)  
RX(64) D + I ==> Y

10/569486

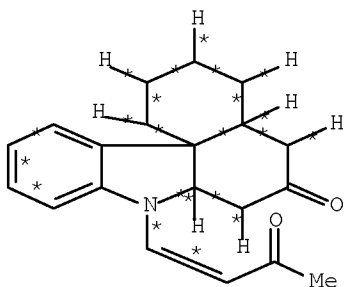


D



I

4  
STEPS  
➔



Y  
YIELD 47%

RX(2)      RCT   D 2646-01-7  
             RGT   F 7647-01-0 HCl  
             PRO   E 2398-19-8  
             SOL   67-56-1 MeOH

RX(3)      RCT   E 2398-19-8  
             RGT   F 7647-01-0 HCl  
             PRO   H 69393-74-4  
             SOL   67-56-1 MeOH

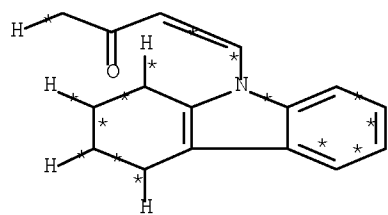
RX(5)      RCT   H 69393-74-4, I 5436-21-5  
             RGT   F 7647-01-0 HCl  
             PRO   J 2398-25-6

RX(12)     RCT   J 2398-25-6  
             RGT   X 7727-43-7 BaSO4  
             PRO   Y 72181-58-9

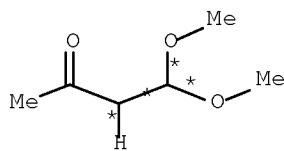
RX(65) OF 67 COMPOSED OF RX(2), RX(3), RX(18), RX(25)  
RX(65)      D   +   I   ==>   AN



10/569486

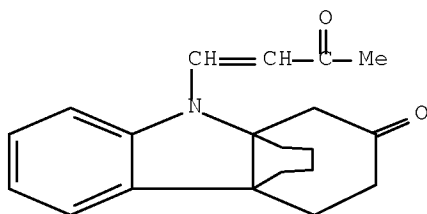


D



I

4  
STEPS  
➔



AN  
YIELD 63%

RX(2)	RCT	D 2646-01-7
	RGT	F 7647-01-0 HCl
	PRO	E 2398-19-8
	SOL	67-56-1 MeOH
RX(3)	RCT	E 2398-19-8
	RGT	F 7647-01-0 HCl
	PRO	H 69393-74-4
	SOL	67-56-1 MeOH
RX(18)	RCT	H 69393-74-4
	RGT	X 7727-43-7 BaSO4
	PRO	AG 72181-70-5
RX(25)	RCT	AG 72181-70-5, I 5436-21-5
	RGT	F 7647-01-0 HCl
	PRO	AN 72181-73-8

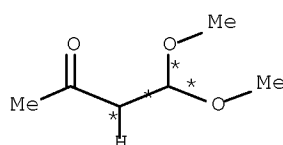
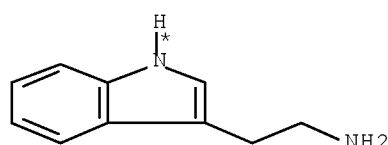
L46 ANSWER 22 OF 24 CASREACT COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 60:52625 CASREACT Full-text  
 TITLE: Syntheses of heterocycles with hydroxymethylene ketones. IV. A new condensation product from tryptamine and acetoacetaldehyde  
 AUTHOR(S): Teuber, Hans Joachim; Glosauer, Otto; Hochmuth, Udo  
 CORPORATE SOURCE: Univ. Frankfurt, Germany  
 SOURCE: Chemische Berichte (1964), 97(2), 557-62  
 CODEN: CHBEAM; ISSN: 0009-2940  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Unavailable

10/569486

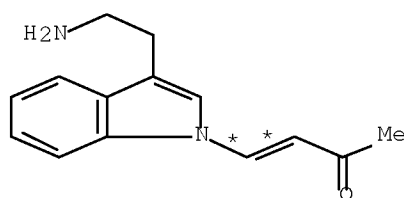
GI For diagram(s), see printed CA Issue.

AB cf. CA 58, 13905c; 59, 15247e. Tryptamine-HCl (I.HCl) with a small amount concentrated HCl and AcCH<sub>2</sub>CH(OMe)<sub>2</sub> (II) yielded 70% III.HCl, m. 193-4° (decomposition). I and II in dilute H<sub>2</sub>SO<sub>4</sub> heated 0.5 hr. at 70-80° gave 1,3,5-C<sub>6</sub>H<sub>3</sub>Ac<sub>3</sub> (IV), needles, m. 161-3° (80% EtOH), and a yellow oil which in MeOH with aqueous KNCO yielded the urea derivative (V) of I, prisms, m. 204-7° (decomposition) III.HCl with 2N NaOH gave about 30% yellow-brown prisms, III, decompose 103-7° (1:1 Me<sub>2</sub>CO-C<sub>6</sub>H<sub>6</sub>), which changed during several months to a viscous brown resin; III gave a deep red color in concentrated H<sub>2</sub>SO<sub>4</sub>; picrate m. 202-6° (EtOH); urea derivative, prisms, decompose 206-8° (MeOH); phenylurea derivs., prisms, decomposing 220-2° (EtOH); N-Ac derivative, needles, m. 154-5° (hot H<sub>2</sub>O); 2,4-dinitrophenylhydrazone, dark red prisms, m. above 260°; oxime, pale yellow needles, decompose 196-8° (EtOH). III.HCl in absolute MeOH treated 2 days at 20° with saturated HClMeOH and then with 10% NaOH gave I, decomposing 145-6°; I.HCl, m. 244-6° (EtOH). The attempted reduction of III.HCl with NaBH<sub>4</sub> in 90% EtOH gave only an unidentified crystalline product, pale yellow in concentrated H<sub>2</sub>SO<sub>4</sub>. III.HCl and methylal in AcOH refluxed 24 hrs. yielded about 80% tetrahydronorharman- HCl.0.5H<sub>2</sub>O (VI.HCl.0.5H<sub>2</sub>O), decompose 254-6° with a color change to red-brown; picrate m. 244-9° (decomposition). VI.HCl with aqueous NaHCO<sub>3</sub> yielded VI, m. 203-5° (C<sub>6</sub>H<sub>6</sub>), and IV, m. 162-3°. The ultraviolet absorption spectrum of I.HCl is recorded.

RX(1) OF 2 A + B ==> C



(1) →



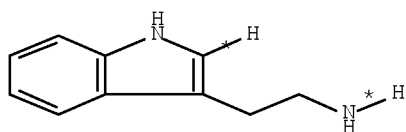
YIELD 70%

RX(1) RCT A 61-54-1, B 5436-21-5  
 RGT D 7647-01-0 HCl  
 PRO C 92255-25-9  
 SOL 7732-18-5 Water  
 NTE Classification: Elimination; N-Alkylation; # Conditions:  
 MeCOCH<sub>2</sub>CH(OMe)<sub>2</sub>; HCl 5-10mn; # Comments: reactant and product

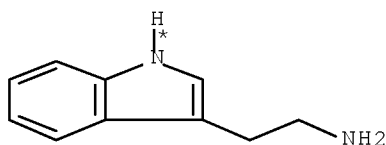
10/569486

are chloride salts

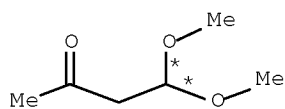
RX(2) OF 2 2 A + 2 B ==> F + G



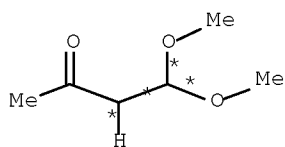
A



A

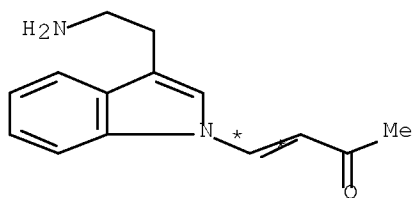


B

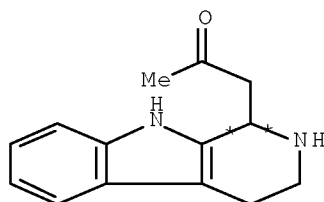


B

(2) →



F



G  
YIELD 70%

RX(2) RCT A 61-54-1, B 5436-21-5  
RGT D 7647-01-0 HCl  
PRO F 157103-25-8, G 69225-88-3  
NTE Classification: Heterocycle formation; Condensation;  
N-Alkylation; Elimination; # Conditions: HCl 5-10mn; # Comments:  
Pictet-Spengler reaction; reactant and product as hydrochloride  
salts; tricyclic minor product

L46 ANSWER 23 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 59:82171 CASREACT Full-text

TITLE: N-Substitution of indoles with hydroxymethylene  
ketones

AUTHOR(S): Teuber, Hans Joachim; Cornelius, Dieter; Pfaff,  
Herbert

CORPORATE SOURCE: Univ. Frankfurt, Germany  
 SOURCE: Chemische Berichte (1963), 96(10), 2617-31  
 CODEN: CHBEAM; ISSN: 0009-2940

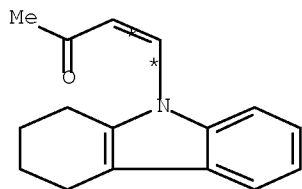
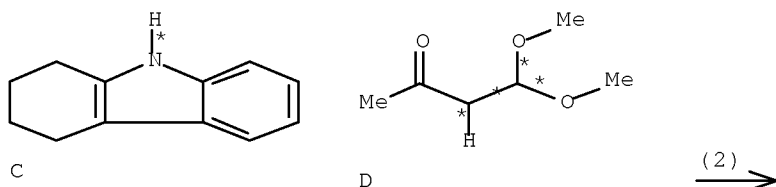
DOCUMENT TYPE: Journal  
 LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

AB Indoles with protected 2- and 2,3-positions react with  $\text{AcCH}_2\text{H}(\text{OEt})_2$  (I) and  $\text{EtOCH:CHCH}(\text{OEt})_2$  (II) in the presence of concentrated HCl to yield the corresponding 1-AcCH:CH and 1-OHCCH:CH derivs., which are reduced by  $\text{NaBH}_4$  to acid-sensitive dihydro derivs. with an allyl alc. function, and over Raney Ni to tetrahydro derivs. with a saturated 1-substituent. The combination of condensation and reduction constitutes a simple method for the N-alkylation of indoles. Skatole reacted beyond the 1-substituted derivative Dihydroindoles, such as 5-acety lindoline (III) and hexahydrocarbazole (IV), react in the same manner as the indoles, but the condensation products differ, because of the greater basicity of the N, from the corresponding compds. in the indole series in their reactive and spectroscopic behavior. The course of the condensation reaction and its relations to alkaloid chemistry are discussed. 1,2,3,4-Tetrahydrocarbazole (V) (5 g.) in 10 cc. I stirred 17-18 min. with 2 cc. concentrated HCl, diluted with  $\text{H}_2\text{O}$ , and filtered, and the residue recrystd. from 30 cc. EtOH yielded 6 g. AcCH:CH derivative (VI) of V, ivory-colored rods and prisms, m.  $127-9^\circ$ ; it is cleaved by 12N HCl even at  $20^\circ$ . VI (480 mg.) and 280 mg.  $\text{NH}_2\text{OH}\cdot\text{HCl}$  in 15 cc.  $\text{C}_5\text{H}_5\text{N}$  kept overnight and diluted with  $\text{H}_2\text{O}$  gave the oxime, decomposing  $191-2^\circ$  (EtOH). VI (480 mg.) in 20 cc.  $\text{C}_5\text{H}_5\text{N}$  kept overnight with 480 mg.  $\text{H}_2\text{NCONHNH}_2\cdot\text{HCl}$  in 1 cc.  $\text{H}_2\text{O}$  gave the semicarbazone, needles, m.  $183-5^\circ$  (MeOH). VI (360 mg.) in 50 cc. MeOH kept overnight with 360 mg.  $\text{NaBH}_4$ , diluted with  $\text{H}_2\text{O}$ , and extracted with Et<sub>2</sub>O gave the N-MeCH(OH)CH:CH derivative (VII) of V, m.  $85-6^\circ$  (ligroine, b.  $50-80^\circ$ ). VI (240 mg.) in 20 cc. MeOH hydrogenated 5 hrs. over Raney Ni gave the NMeCH(OH)CH<sub>2</sub>CH<sub>2</sub> derivative (VIII) of V, m.  $80-2^\circ$  (ligroine). 1-Me derivative (1.85 g.) of V, 4 cc. I, and 1 cc. concentrated HCl yielded in the usual manner the 1-Me derivative of N-(3-oxo-1-butenyl)-1,2,3,4-tetrahydrocarbazole (IX), ivory-colored crystals, m.  $118^\circ$  (EtOH); oxime m.  $177-8^\circ$  (decomposition) (EtOH). V (1.7 g.) in 5 cc. II treated with 5 drops concentrated HCl and diluted after 2-3 min. with  $\text{H}_2\text{O}$  gave 70-80% N-OHCCH:CH derivative (X) of V, orange needles, re.  $132^\circ$  (EtOH). X (225 mg.) and 140 mg.  $\text{NH}_2\text{OH}\cdot\text{HCl}$  in 10 cc.  $\text{C}_5\text{H}_5\text{N}$  gave during 5 hrs. the oxime, pale yellow needles, m.  $158^\circ$ . 1-OH derivative (560 mg.) of V, 2 cc. I, and 10 drops concentrated HCl gave octahydro[1,9:9',1']bicarbazolyene, m.  $275-8^\circ$  ( $\text{C}_6\text{H}_6$ ). Carbazole (XI) (5.0 g.), 10 cc. I, and 2 cc. concentrated HCl stirred 15 min. and diluted with  $\text{H}_2\text{O}$  yielded 6.3 g. N-AcCH:CH derivative (XII) of XI, m.  $138-9^\circ$  (EtOH). XII (235 mg.) in 50 cc. 12N HCl diluted after 1 hr. with  $\text{H}_2\text{O}$  gave XI. XII (350 mg.) treated overnight with 210 mg.  $\text{NH}_2\text{OH}\cdot\text{HCl}$  in 10 cc.  $\text{C}_5\text{H}_5\text{N}$  yielded the oxime, m.  $176-7^\circ$  (decomposition) (EtOH). XII (350 mg.) in 50 cc. MeOH treated overnight with 350 mg.  $\text{NaBH}_4$  yielded N-(3-hydroxy-1-butenyl)carbazole (XIII), needles, m.  $104-5^\circ$ . XI (1.7 g.), 3 cc. II, 2 cc. EtOH, and 3 drops concentrated HCl stirred about 3 min. yielded 900 mg. N-OHCCH:CH derivative (XIV) of XI, pale yellow needles, m.  $156^\circ$  (EtOH). XIV (220 mg.), 140 mg.  $\text{NH}_2\text{OH}\cdot\text{HCl}$ , and 10 cc.  $\text{C}_5\text{H}_5\text{N}$  kept overnight yielded the oxime, m.  $164-7^\circ$  (EtOH). XIV (330 mg.) in 50 cc. MeOH kept overnight with  $\text{NaBH}_4$  gave a mixture of N- $\text{HOCH}_2\text{CH:CH}$  derivative (XV) of XI and XI, m.  $200-5^\circ$ , with sintering at  $120-5^\circ$ . 1-Hydroxycarbazole (XVI) (1.85 g.), m.  $158^\circ$ , in 4 cc. I and 1 cc. concentrated HCl stirred 15 min. and diluted with  $\text{H}_2\text{O}$  gave over 90% N-AcCH:CH derivative (XVII) of XVI, m.  $203-4^\circ$  (EtOH). A similar run with com. 2-hydroxycarbazole (apparently containing XVI) gave after standing overnight a dark resin; this, powdered, dissolved in  $\text{Me}_2\text{CO}$ , filtered through  $\text{Al}_2\text{O}_3$ , and evapd, gave XIII, m.  $205-6^\circ$  (EtOH); further elution of the column with MeOH, evaporation of the eluate, and chromatography of the residue again on  $\text{Al}_2\text{O}_3$  gave a blue solid,  $\text{C}_{32}\text{H}_{28}\text{N}_2\text{O}_5$ , m.  $150-6^\circ$ , after sintering from  $90^\circ$ .

2,3-Dimethylindole (1.45 g.), 3 cc. I, and 0.5 cc. concentrated HCl stirred 15 min. and diluted with H<sub>2</sub>O yielded over 95% 1-AcCH:CH derivative (XVIII), pale yellow crystals, m. 110° (aqueous EtOH). XVIII (320 mg.) with 210 mg. NH<sub>2</sub>OH.HCl in 10 cc. C<sub>5</sub>H<sub>5</sub>N gave overnight the oxime, m. 171-4° (decomposition) (EtOH). Skatole (3.9 g.) in 10 cc. I stirred 0.5 (and 1) hr. with 2 cc. concentrated HCl, diluted with H<sub>2</sub>O, and decanted, the residual resin triturated with H<sub>2</sub>O, dried on a clay plate, dissolved in C<sub>6</sub>H<sub>6</sub>, and chromatographed on Al<sub>2</sub>O<sub>3</sub> gave a small amount of 3-methyl-N-(3-oxo-1-butenyl)indole, m. 176-8° (MeOH). Skatole (10 g.) and 15 cc. I treated during 75 min. with stirring with 20 cc. 6N HCl, diluted with H<sub>2</sub>O, and decanted, and the dried, resinous residue extracted with Et<sub>2</sub>O left 2.8 g. brown powder, which yielded from EtOAc yellow-brown needles. IV (850 mg.), 2 cc. I, and 1 cc. concentrated HCl kept 0.5 hr. and diluted with H<sub>2</sub>O yielded 800 mg. N-AcCH:CH derivative (XIX) of IV, yellowish prisms, m. 125°. XIX and NH<sub>2</sub>OH.HCl in C<sub>5</sub>H<sub>5</sub>N kept overnight yielded IV, m. 98-9°. XIX in MeOH was not affected by NaBH<sub>4</sub>. Indoline and III with I gave similarly the 1-AcCH:CH derivs., m. 100° (ligroine), and 180° (EtOH), resp. N-Methyl-1,2,3,4-tetrahydrocarbazole, 11-methyl-1,2,3,4-tetrahydrocarbazolenine, and 1- and 4-oxo-1,2,3,4-tetrahydrocarbazole did not react with I and concentrated HCl; in some cases some 1,3,5-C<sub>6</sub>H<sub>3</sub>Ac<sub>3</sub>, m. 161° (H<sub>2</sub>O), was obtained. V did not react with Me<sub>2</sub>CO, Ac<sub>2</sub>CH<sub>2</sub>, or AcCH<sub>2</sub>CO<sub>2</sub>Et under the same conditions as I, not even in refluxing EtOH in the presence of concentrated HCl. The ultraviolet spectra of VI, VII, VIII, IX, X, XII, XIII, XIV, XV, XVII, and XIX, and the infrared spectra in the 5.5-6.5 μ region of VI, VII, X, XII, and XIX are recorded.

RX(2) OF 3      C + D ==> E



E  
YIELD 85%

RX(2)      RCT    C 942-01-8, D 5436-21-5  
              PRO    E 2646-01-7  
              SOL    7647-01-0 HCl  
              NTE    Classification: Elimination; Geoselectiveintermediate;

N-Alkylation; # Conditions: MeCOCH<sub>2</sub>CH(OMe)<sub>2</sub>; HCl 2-3mn + 15mn

L46 ANSWER 24 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 34:35971 CASREACT [Full-text](#)

TITLE: Preparation of  $\alpha,\beta$ -dichloroethylanisoles  
and transformation to  $\alpha$ - and  
 $\beta$ -chloromethoxystyrenes

AUTHOR(S): Quelet, Raymond; Allard, Jean

SOURCE: Bull. soc. chim. (1940), 7, 215-27

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

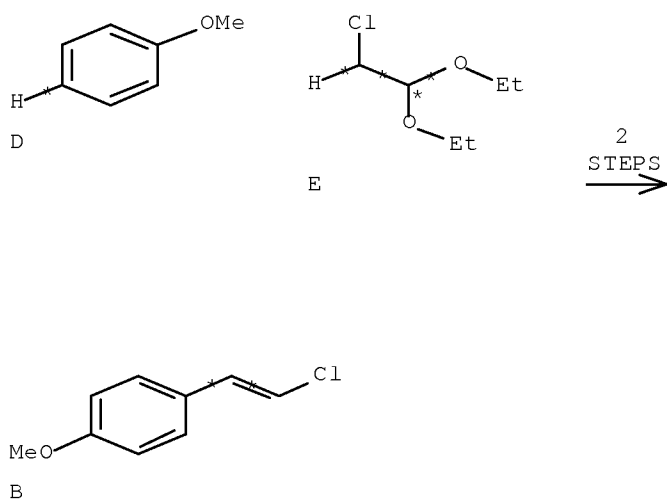
AB A mixture of 108 g. anisole, 152 g. of ClCH<sub>2</sub>CH(OEt)<sub>2</sub>, 100 g. of concentrated HCl and 50 g. H<sub>2</sub>O was stirred for 2 hrs. at 60-70° in the presence of dry HCl. The reaction product was washed, dried and freed from unreacted anisole and ClCH<sub>2</sub>CH(OEt)<sub>2</sub> by rapid distillation in vacuo, yielding 32% of crude  $\alpha,\beta$ -dichloroethylanisole (I). A mixture of I with 100 g. pyridine was heated for 6 hrs. at 115°, treated with dilute HCl, washed and extracted with ether. The dried extract was distilled, producing 55 g. of crude p-methoxy- $\beta$ -chlorostyrene (II) and 20 g. of crystalline residue (III). II gave 20 g. of solid crystals, which on recrystn. from alc. gave brilliant white platelets of pure II, C<sub>9</sub>H<sub>9</sub>ClO, m. 32°, n<sub>D</sub>35 1.5820, and 35 g. of a liquid mixture, b<sub>16</sub> 133-5°, n<sub>D</sub>20 1.5720, n<sub>D</sub>35 1.5625, consisting of II and a trace of a non-chlorinated derivative. Recrystn. of III from benzene produced white platelets of 4,4'-dimethoxystilbene, m. 212°. Treatment of I with 2 mols. of NaOEt in absolute alc. for 4 hrs. at 100°, evaporation, dilution with H<sub>2</sub>O, extraction with ether and distillation gave 40 g. anisole, 60 g. of crude p-methoxy- $\alpha$ -chlorostyrene (IV) and 20 g. of residue (V), b<sub>16</sub> above 170°. On cooling, the crude IV gave 45 g. of pure IV, m. 45°, decomposing on standing with evolution of HCl and formation of a resin which, on steam distillation, gave p-MeOC<sub>6</sub>H<sub>4</sub>Ac, m. 35°, a red powder and a resin, m. 70°. IV was reduced catalytically to p-ethylanisole. Recrystn. of V from benzene produced  $\alpha,\alpha$ -bis(4-methoxyphenyl)ethylene (VI), m. 143° oxidized by K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub> to 4,4'-dimethoxybenzophenone, m. 144°. Treatment of I with 112 g. KOH in 100 g. H<sub>2</sub>O and 300 g. of 95% alc. for 4 hrs. at 100°, evaporation, dilution with H<sub>2</sub>O, extraction with ether and filtration gave 17 g. VI, insol. in ether. Evaporation and fractional distillation of the extract yielded 11 g. anisole; 34 g. IV; 30 g. of p-methoxy( $\alpha$ -ethoxy- $\beta$ -chloroethyl)benzene (VII), b<sub>16</sub> 145-8°, d<sub>4</sub>20 1.113, n<sub>D</sub>20 1.5230; and a residue of 25 g. of VI. Treatment of 1 mol. I with 70 g. KCN in 100 g. H<sub>2</sub>O and 250 g. of 95% alc. by heating to boiling and refluxing for 1 hr. after the exothermic reaction gave 40 g. anisole; 5 g. of a product, b<sub>15</sub> 120-30°, n<sub>D</sub>20 1.5080; 10 g. of residual 4,4'-dimethoxystilbene, m. 212°, and 53 g. of a fraction, b<sub>16</sub> 145-50°, n<sub>D</sub>20 1.5250, which was refractionated to yield 30 g. VII, pyrolyzed to give 70% of II, converted by boiling for 3 hrs. with alc. NaOEt to p-methoxy- $\alpha$ -ethoxystyrene, b<sub>16</sub> 135-7°, n<sub>D</sub>20 1.5395, d<sub>4</sub>20 1.050, catalytically reduced in the presence of PtO<sub>2</sub> to p-ethylanisole, b<sub>16</sub> 83-5°, n<sub>D</sub>20 1.5100, and mainly to p-methoxy- $\alpha$ -ethoxyethylbenzene, b<sub>16</sub> 114-15°, n<sub>D</sub>20 1.5080, d<sub>4</sub>20 0.995. Extension of the method of condensation of ClCH<sub>2</sub>CH(OEt)<sub>2</sub> to other phenolic ethers gave only 5% yields of the corresponding  $\alpha,\beta$ -di-Cl compds. These are preferably made in 25% yields by chlorination of the corresponding methoxystyrenes obtained by dechlorohydration of the  $\alpha$ -chloroethyl homologs of anisole: 3-methyl-4-methoxy- $\alpha$ -chlorostyrene, b<sub>18</sub> 145-50°, n<sub>D</sub>20 1.5650, d<sub>4</sub>20 1.163; 3-methyl-4-methoxy- $\beta$ -chlorostyrene, b<sub>18</sub> 155-8°, m. 65.5°; 5-methyl-2-methoxy- $\alpha$ -chlorostyrene, b<sub>16</sub> 135-7°, n<sub>D</sub>20 1.5488, d<sub>4</sub>20 1.113; 5-methyl-2-methoxy- $\beta$ -chlorostyrene, b<sub>16</sub> 143-5°, n<sub>D</sub>20 1.5715, d<sub>4</sub>20 1.178; 2-methyl-5-isopropyl-4-

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methoxy- $\alpha$ -chlorostyrene, b16 158-60°, nD20 1.5230 (in this reaction there is also produced an appreciable amount of 2-methyl-5-isopropyl-4-methoxy-1-( $\alpha$ -ethoxy- $\beta$ -chloroethyl)benzene, b16 164-5°, nD20 1.5260, pyrolyzed to the corresponding  $\beta$ -chlorostyrene, b16 155-60°, nD20 1.5578, d420 1.095. There is also formed some amount of a compound, probably 2-methyl-5-isopropyl-4-methoxy- $\alpha$ -ethoxystyrene, b16 145-50°, nD20 1.5235.)

RX(4) OF 5 COMPOSED OF RX(2), RX(1)

RX(4) D + E ==> B



RX(2) RCT D 100-66-3, E 621-62-5  
 RGT F 7647-01-0 HCl  
 PRO A 119015-52-0  
 SOL 7732-18-5 Water  
 NTE Classification: C-Alkylation; Chlorination; Regioselective; #  
 Conditions: H2O HCl saturated; 60-70 deg 2h; # Comments: other  
 examples with lower yields; ZnCl2 or H3PO4 gives a poorer yield

RX(1) RCT A 119015-52-0  
 RGT C 110-86-1 Pyridine  
 PRO B 18684-94-1  
 NTE Classification: Elimination; Dehydrochlorination; # Conditions:  
 pyridine

=> file registry

FILE 'REGISTRY' ENTERED AT 14:17:10 ON 08 SEP 2008  
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DICTIONARY FILE UPDATES: 7 SEP 2008 HIGHEST RN 1047406-12-1

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FILE CONTENT:1840 - 31 Aug 2008 VOL 149 ISS 10

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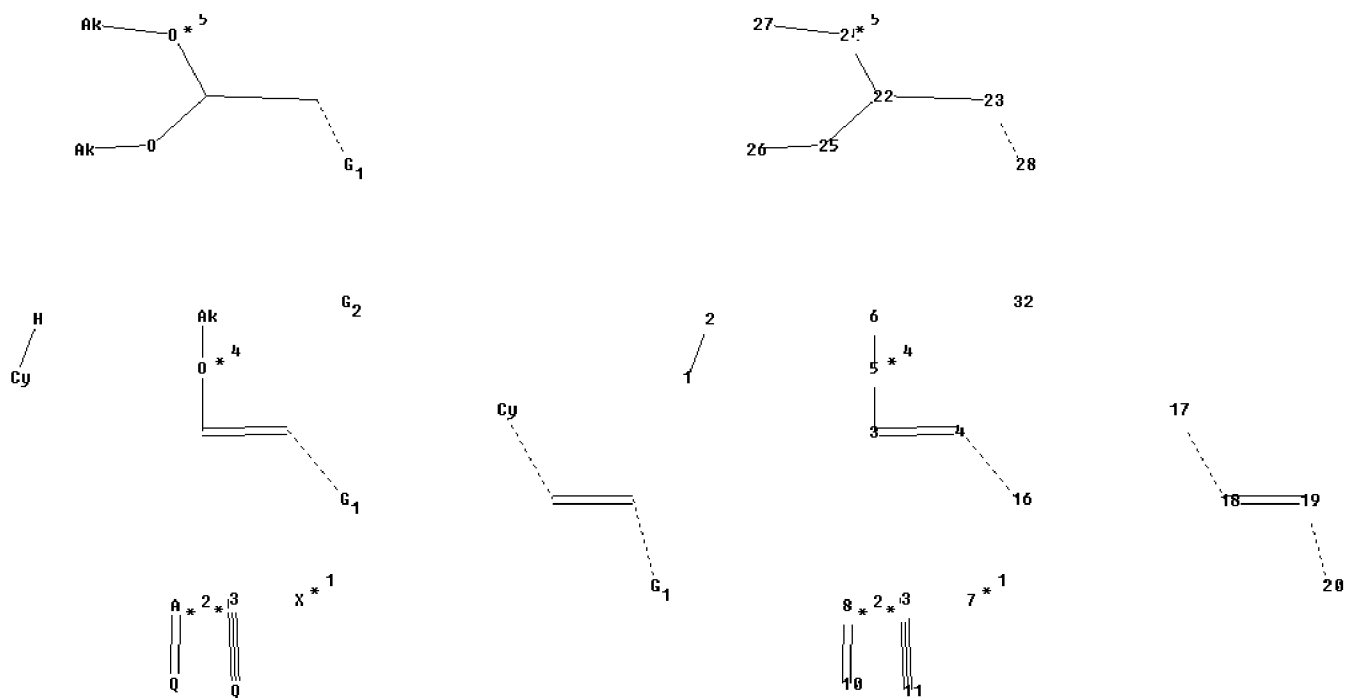
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10/569486



chain nodes :

1 2 3 4 5 6 7 16 17 18 19 20 22 23 24 25 26 27 28 32

ring/chain nodes :

8 9 10 11

chain bonds :

1-2 3-4 3-5 4-16 5-6 17-18 18-19 19-20 22-23 22-24 22-25 23-28 24-27  
25-26

ring/chain bonds :

8-10 9-11

exact/norm bonds :

1-2 3-5 4-16 5-6 8-10 9-11 17-18 19-20 22-24 22-25 23-28 24-27 25-26

exact bonds :

3-4 18-19 22-23

G1:[\*1],[\*2],[\*3]

G2:[\*4],[\*5]

Match level :

1:Atom 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS

10:CLASS

11:CLASS 16:CLASS 17:Atom 18:CLASS 19:CLASS 20:CLASS 22:CLASS 23:CLASS

24:CLASS 25:CLASS

26:CLASS 27:CLASS 28:CLASS 32:CLASS

Generic attributes :

1:

Saturation : Unsaturated

17:

Saturation : Unsaturated

fragments assigned reactant role:

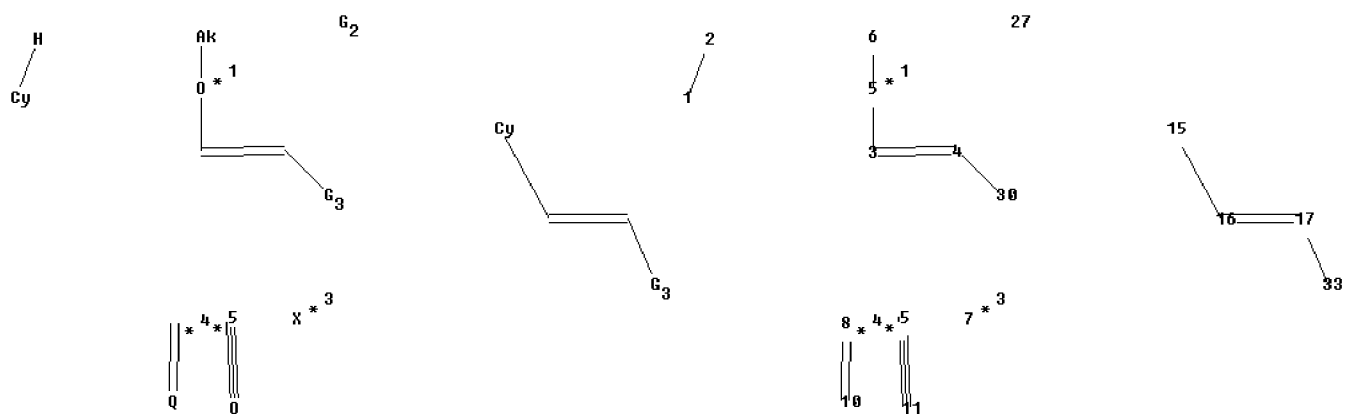
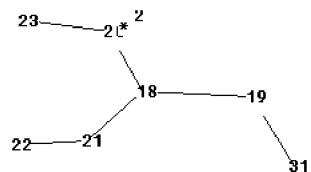
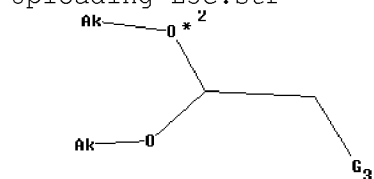
containing 1

containing 32

10/569486

fragments assigned product role:  
 containing 17  
 reaction site bonds:  
 17-18:CC

Uploading L5c.str



chain nodes :

1 2 3 4 5 6 7 8 9 10 11 15 16 17 18 19 20 21 22 23 27 30 31  
 33

chain bonds :

1-2 3-4 3-5 4-30 5-6 8-10 9-11 15-16 16-17 17-33 18-19 18-20 18-21 19-31  
 20-23 21-22

exact/norm bonds :

1-2 3-5 4-30 5-6 8-10 9-11 15-16 17-33 18-20 18-21 19-31 20-23 21-22

exact bonds :

3-4 16-17 18-19

G2:[\*1],[\*2]

G3:[\*3],[\*4],[\*5]

Hydrogen count :

3:= exact 1 4:= exact 1 16:= exact 1 17:= exact 1 18:= exact 1 19:= exact 2

Connectivity :

3:2 E exact RC ring/chain 4:2 E exact RC ring/chain 16:2 E exact RC ring/chain  
 17:2 E exact RC ring/chain 18:3 E exact RC ring/chain 19:2 E exact RC ring/chain

Match level :

1:Atom 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS  
 10:CLASS

10/569486

11:CLASS 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS  
22:CLASS 23:CLASS  
27:CLASS 30:CLASS 31:CLASS 33:CLASS  
Generic attributes :

1:  
Saturation : Unsaturated  
15:  
Saturation : Unsaturated

fragments assigned reactant role:  
containing 1  
containing 27  
fragments assigned product role:  
containing 15  
reaction site bonds:  
15-16:CC

=> d stat que L22  
L1 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.  
L2 ( 190274)SEA FILE=CASREACT ABB=ON PLU=ON ACYCLIC ALKENE/FG.PRO  
L3 SCR 278 OR 1342  
L4 143 SEA FILE=CASREACT SUB=L2 SSS FUL L1 AND L3 ( 742 REACTIONS)  
L5 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.  
L7 43 SEA FILE=CASREACT SUB=L4 SSS FUL L5 ( 207 REACTIONS)  
L8 TRANSFER PLU=ON L4 1- RX : 1312 TERMS  
L9 1312 SEA FILE=REGISTRY ABB=ON PLU=ON L8/RN  
L10 441 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND X/ELS  
L11 421 SEA FILE=REGISTRY ABB=ON PLU=ON L10 AND C/ELS  
L12 20 SEA FILE=REGISTRY ABB=ON PLU=ON L10 NOT L11  
L13 188275 SEA FILE=CASREACT ABB=ON PLU=ON L12  
L14 24 SEA FILE=CASREACT ABB=ON PLU=ON L13 (L) L7  
L16 11 SEA FILE=REGISTRY ABB=ON PLU=ON L12 AND M/ELS  
L17 9 SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L16  
L18 153759 SEA FILE=CASREACT ABB=ON PLU=ON L17  
L19 31 SEA FILE=CASREACT ABB=ON PLU=ON L18 (L) L4  
L22 16 SEA FILE=CASREACT ABB=ON PLU=ON L19 NOT L14

=> d stat que L43  
L1 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.  
L2 ( 190274)SEA FILE=CASREACT ABB=ON PLU=ON ACYCLIC ALKENE/FG.PRO  
L3 SCR 278 OR 1342  
L4 143 SEA FILE=CASREACT SUB=L2 SSS FUL L1 AND L3 ( 742 REACTIONS)  
L8 TRANSFER PLU=ON L4 1- RX : 1312 TERMS  
L9 1312 SEA FILE=REGISTRY ABB=ON PLU=ON L8/RN

10/569486

```
L10      441 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND X/ELS
L11      421 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND C/ELS
L12      20  SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 NOT L11
L16      11  SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND M/ELS
L17      9   SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 NOT L16
L18      153759 SEA FILE=CASREACT ABB=ON  PLU=ON  L17
L19      31  SEA FILE=CASREACT ABB=ON  PLU=ON  L18 (L) L4
L37      75833 SEA FILE=CASREACT ABB=ON  PLU=ON  64-19-7
L43      7   SEA FILE=CASREACT ABB=ON  PLU=ON  L37 (L) L19
```

=> s L22 or L43

L47 18 L22 OR L43

=> s L47 not L46

L48 16 L47 NOT L46

=> d ibib abs hit L48 1-16

L48 ANSWER 1 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 146:441705 CASREACT Full-text

TITLE: Regiospecific preparation of 1,4,5-trisubstituted  
pyrazoles from 2-(1H-1,2,3-benzotriazol-1-yl)-3-(4-  
aryl)-2-propenal derivatives

AUTHOR(S): Katritzky, Alan R.; Vakulenko, Anatoliy V.; Akue-Gedu,  
Rufine; Gromova, Anna V.; Witek, Rachel; Rogers, James  
W.

CORPORATE SOURCE: Center for Heterocyclic Compounds, Department of  
Chemistry, University of Florida, Gainesville, FL,  
32611-7200, USA

SOURCE: ARKIVOC (Gainesville, FL, United States) (2007), (1),  
9-21

CODEN: AGFUAR

URL: <http://content.arkat->

usa.org/ARKIVOC/JOURNAL\_CONTENT/manuscripts/2007/07-  
2282DP%20as%20published%20mainmanuscript.pdf

PUBLISHER: Arkat USA Inc.

DOCUMENT TYPE: Journal; (online computer file)

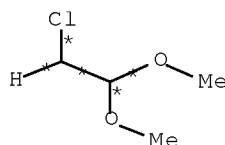
LANGUAGE: English

AB Treatment of  $\alpha$ -(benzotriazolyl)- $\alpha,\beta$ -unsatd. aldehydes with monosubstituted  
hydrazine derivs., followed by alkylation at the 4-position of the pyrazoline  
ring and elimination of the benzotriazole group affords 1,4,5-trisubstituted  
pyrazoles in overall yields of 52-79%.

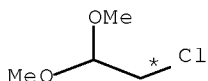
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(68) OF 112 COMPOSED OF RX(1), RX(2), RX(8)

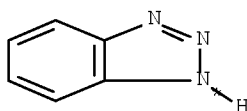
RX(68) 2 A + B + C + H ==> Y



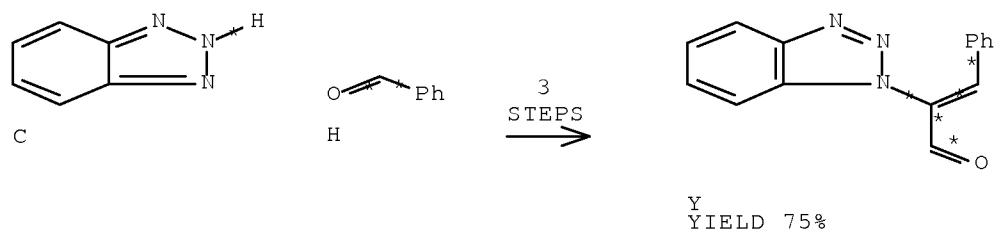
A



A



B



```

RX(1)      RCT  A 97-97-2, B 95-14-7, C 273-02-9
           RGT  F 298-14-6 KHCO3
           PRO  D 304690-46-8, E 304690-47-9
           SOL  68-12-2 DMF
           CON  SUBSTAGE(1) 18 hours, reflux
                SUBSTAGE(2) cooled

RX(2)      RCT  D 304690-46-8

           STAGE(1)
             RGT  J 109-72-8 BuLi
             SOL  109-99-9 THF, 110-54-3 Hexane
             CON  SUBSTAGE(1) -78 deg C
                   SUBSTAGE(2) 1 hour, -78 deg C

           STAGE(2)
             RCT  H 100-52-7
             SOL  109-99-9 THF
             CON  SUBSTAGE(1) -78 deg C
                   SUBSTAGE(2) 2 hours, -78 deg C -> room temperature

           STAGE(3)
             RGT  K 12125-02-9 NH4Cl
             SOL  7732-18-5 Water
             CON  room temperature

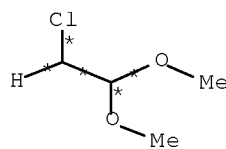
           PRO  I 934565-49-8
           NTE  stereoselective, 70:30 E:Z

RX(8)      RCT  I 934565-49-8
           RGT  Z 7647-01-0 HCl
           PRO  Y 161373-60-0
           SOL  7732-18-5 Water, 109-99-9 THF
           CON  SUBSTAGE(1) room temperature
                SUBSTAGE(2) 48 hours, room temperature
           NTE  stereoselective

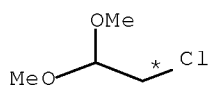
RX(69) OF 112 COMPOSED OF RX(1), RX(3), RX(10)
RX(69)      2 A + E + C + O ==> AE

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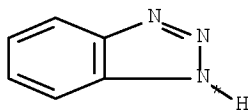
10/569486



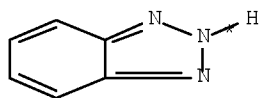
A



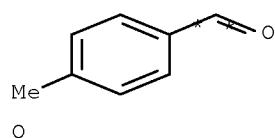
A



B

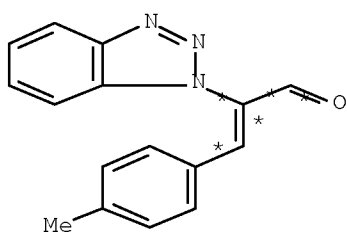


C



O

3  
STEPS  
→



AB  
YIELD 95%

RX(1) RCT A 97-97-2, B 95-14-7, C 273-02-9  
RGT F 298-14-6 KHCO<sub>3</sub>  
PRO D 304690-46-8, E 304690-47-9  
SOL 68-12-2 DMF  
CON SUBSTAGE(1) 18 hours, reflux  
SUBSTAGE(2) cooled

RX(3) RCT D 304690-46-8

STAGE(1)

RGT J 109-72-8 BuLi  
SOL 109-99-9 THF, 110-54-3 Hexane  
CON SUBSTAGE(1) -78 deg C  
SUBSTAGE(2) 1 hour, -78 deg C

STAGE(2)

RCT O 104-87-0  
SOL 109-99-9 THF  
CON SUBSTAGE(1) -78 deg C  
SUBSTAGE(2) 2 hours, -78 deg C -> room temperature

10/569486

STAGE(3)

RGT K 12125-02-9 NH4Cl

SOL 7732-18-5 Water

CON room temperature

PRO P 934565-50-1

NTE stereoselective, 70:30 E:Z

RX(10)

RCT P 934565-50-1

RGT Z 7647-01-0 HCl

PRO AB 934565-56-7

SOL 7732-18-5 Water, 109-99-9 THF

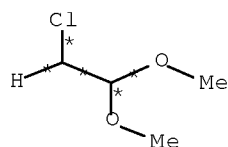
CON SUBSTAGE(1) room temperature

SUBSTAGE(2) 48 hours, room temperature

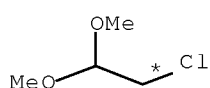
NTE stereoselective

RX(71) OF 112 COMPOSED OF RX(1), RX(5), RX(12)

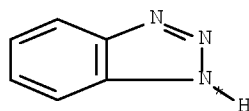
RX(71) 2 A + B + C + S ==> AD



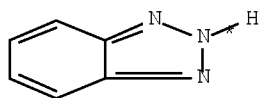
A



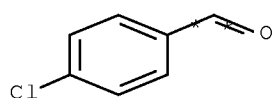
A



B

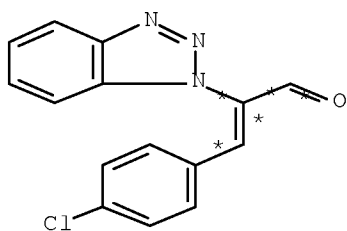


C



S

3  
STEPS  
→



AD  
YIELD 85%

10/569486

RX(1) RCT A 97-97-2, B 95-14-7, C 273-02-9  
 RGT F 298-14-6 KHCO3  
 PRO D 304690-46-8, E 304690-47-9  
 SOL 68-12-2 DMF  
 CON SUBSTAGE(1) 18 hours, reflux  
 SUBSTAGE(2) cooled

RX(5) RCT D 304690-46-8

STAGE(1)  
 RGT J 109-72-8 BuLi  
 SOL 109-99-9 THF, 110-54-3 Hexane  
 CON SUBSTAGE(1) -78 deg C  
 SUBSTAGE(2) 1 hour, -78 deg C

STAGE(2)  
 RCT S 104-88-1  
 SOL 109-99-9 THF  
 CON SUBSTAGE(1) -78 deg C  
 SUBSTAGE(2) 2 hours, -78 deg C -> room temperature

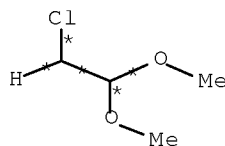
STAGE(3)  
 RGT K 12125-02-9 NH4Cl  
 SOL 7732-18-5 Water  
 CON room temperature

PRO T 934565-52-3  
 NTE stereoselective, 70:30 E:Z

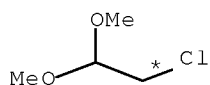
RX(12) RCT T 934565-52-3  
 RGT Z 7647-01-0 HCl  
 PRO AD 161373-55-3  
 SOL 7732-18-5 Water, 109-99-9 THF  
 CON SUBSTAGE(1) room temperature  
 SUBSTAGE(2) 48 hours, room temperature  
 NTE stereoselective

RX(72) OF 112 COMPOSED OF RX(1), RX(6), RX(13)

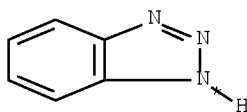
RX(72) 2 A + B + C + U ==> AE



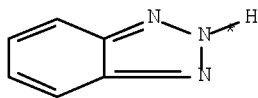
A



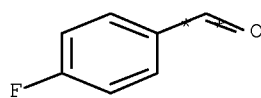
A



B



C

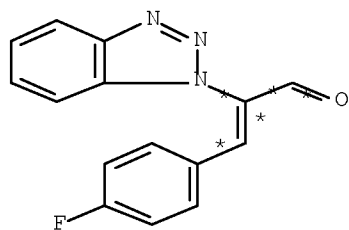


U

3  
STEPS  
→



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AE  
YIELD 90%

RX(1) RCT A 97-97-2, B 95-14-7, C 273-02-9  
RGT F 298-14-6 KHCO<sub>3</sub>  
PRO D 304690-46-8, E 304690-47-9  
SOL 68-12-2 DMF  
CON SUBSTAGE(1) 18 hours, reflux  
SUBSTAGE(2) cooled

RX(6) RCT D 304690-46-8

STAGE(1)  
RGT J 109-72-8 BuLi  
SOL 109-99-9 THF, 110-54-3 Hexane  
CON SUBSTAGE(1) -78 deg C  
SUBSTAGE(2) 1 hour, -78 deg C

STAGE(2)  
RCT U 459-57-4  
SOL 109-99-9 THF  
CON SUBSTAGE(1) -78 deg C  
SUBSTAGE(2) 2 hours, -78 deg C -> room temperature

STAGE(3)  
RGT K 12125-02-9 NH<sub>4</sub>Cl  
SOL 7732-18-5 Water  
CON room temperature

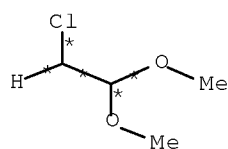
PRO V 934565-53-4  
NTE stereoselective, 70:30 E:Z

RX(13) RCT V 934565-53-4  
RGT Z 7647-01-0 HCl  
PRO AE 161373-56-4  
SOL 7732-18-5 Water, 109-99-9 THF  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 48 hours, room temperature  
NTE stereoselective

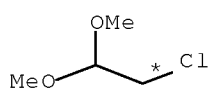
RX(73) OF 112 COMPOSED OF RX(1), RX(7), RX(14)

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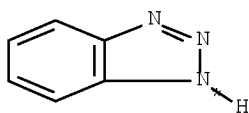
RX(73) 2 A + B + C + W ==> AF



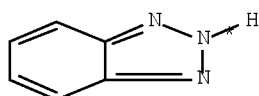
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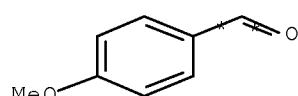
A



B

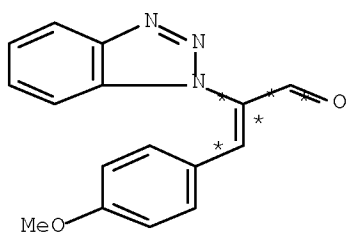


C



W

3  
STEPS  
→



AF  
YIELD 94%

RX(1) RCT A 97-97-2, B 95-14-7, C 273-02-9  
RGT F 298-14-6 KHCO<sub>3</sub>  
PRO D 304690-46-8, E 304690-47-9  
SOL 68-12-2 DMF  
CON SUBSTAGE(1) 18 hours, reflux  
SUBSTAGE(2) cooled

RX(7) RCT D 304690-46-8

STAGE(1)

RGT J 109-72-8 BuLi  
SOL 109-99-9 THF, 110-54-3 Hexane  
CON SUBSTAGE(1) -78 deg C  
SUBSTAGE(2) 1 hour, -78 deg C

STAGE(2)

RCT W 123-11-5  
SOL 109-99-9 THF

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CON SUBSTAGE(1) -78 deg C  
SUBSTAGE(2) 2 hours, -78 deg C -> room temperature

STAGE(3)  
RGT K 12125-02-9 NH4Cl  
SOL 7732-18-5 Water  
CON room temperature

PRO X 934565-54-5  
NTE stereoselective, 70:30 E:Z

RX(14) RCT X 934565-54-5  
RGT Z 7647-01-0 HCl  
PRO AF 934565-58-9  
SOL 7732-18-5 Water, 109-99-9 THF  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 48 hours, room temperature  
NTE stereoselective

L48 ANSWER 2 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 145:489028 CASREACT Full-text

TITLE: Synthesis of rigid trichostatin A analogs as HDAC inhibitors

AUTHOR(S): Charrier, Cedric; Bertrand, Philippe; Gesson, Jean-Pierre; Roche, Joelle

CORPORATE SOURCE: Laboratoire Synthèse et Réactivité des Substances Naturelles, UMR 6514, Université de Poitiers et CNRS, Poitiers, 86022, Fr.

SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(20), 5339-5344  
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

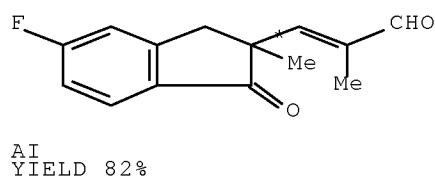
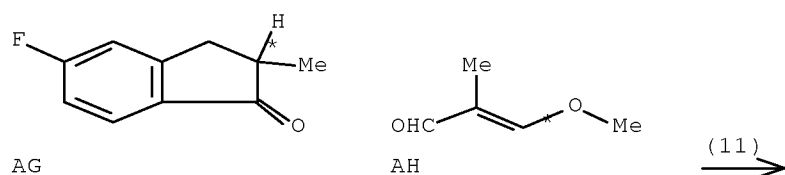
LANGUAGE: English

AB New inhibitors of histone deacetylase (HDAC) have been synthesized and evaluated for their activity toward non small lung cancer cell line H661. Their design is based on indanone (or tetralone) systems leading to trichostatin A (TSA) analogs with limited conformational mobility. Mol. modelization at the AM1 level revealed that the conformations of indane-based analogs and TSA bound to HDAC like protein are similar. The synthesis of these new analogs was achieved by alkylation of an appropriate indanone (or tetralone) to introduce the side chain bearing a terminal ester group, the latter being a precursor of hydroxamic acid and aminobenzamide derivs. Hydroxamic acids with the TSA side chain were found to be the most active compds. and the presence of the dimethylamino group on the Ph ring turned out to be essential to achieve low micromolar activities against H661 cancer cells.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(11) OF 153 ...AG + AB ==> AI...

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RX(11) RCT AG 41201-58-5

STAGE(1)

RGT Q 4111-54-0 LiN(Pr-i)<sub>2</sub>

SOL 109-99-9 THF

CON 1.5 hours, -80 deg C

STAGE(2)

RCT AH 914261-53-3

SOL 109-99-9 THF

CON SUBSTAGE(1) 3 hours, -80 deg C

SUBSTAGE(2) overnight, -80 deg C → room temperature

STAGE(3)

RGT V 12125-02-9 NH<sub>4</sub>Cl

SOL 7732-18-5 Water

STAGE(4)

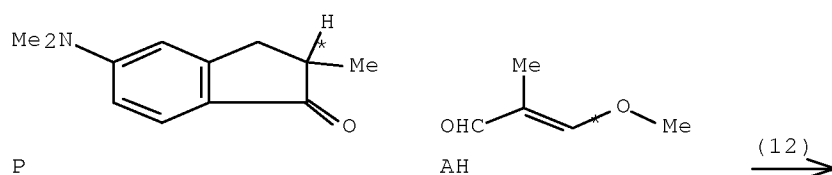
CAT 196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium salt (1:3)

SOL 108-88-3 PhMe

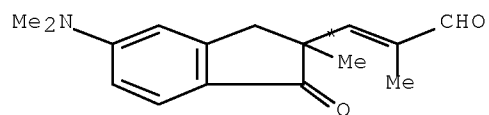
CON 1 hour, reflux

PRO AI 914261-70-4

RX(12) OF 153 ...P + AH ==> AK...



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AK  
YIELD 80%

RX(12) RCT P 914261-49-7

STAGE(1)

RGT Q 4111-54-0 LiN(Pr-i)2

SOL 109-99-9 THF

CON 1.5 hours, -80 deg C

STAGE(2)

RCT AH 914261-53-3

SOL 109-99-9 THF

CON SUBSTAGE(1) 3 hours, -80 deg C

SUBSTAGE(2) overnight, -80 deg C -> room temperature

STAGE(3)

RGT V 12125-02-9 NH4Cl

SOL 7732-18-5 Water

STAGE(4)

CAT 196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium salt (1:3)

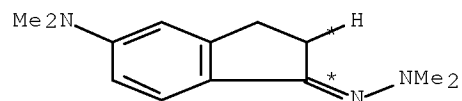
SOL 108-88-3 PhMe

CON 1 hour, reflux

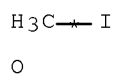
PRO AK 914261-54-4

RX(41) OF 153 COMPOSED OF RX(4), RX(12)

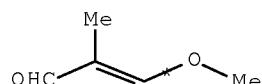
RX(41) L + O + AH ==> AK



L



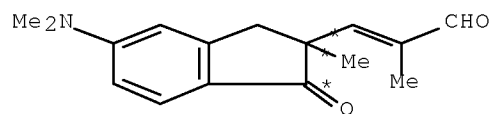
O



AH

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2  
STEPS  
→



AK  
YIELD 80%

RX(4) RCT L 914261-36-2, O 74-88-4

STAGE(1)

RGT Q 4111-54-0 LiN(Pr-i)<sub>2</sub>

CON -40 deg C

STAGE(2)

RGT R 12408-02-5 H<sup>+</sup>

PRO P 914261-49-7

RX(12) RCT P 914261-49-7

STAGE(1)

RGT Q 4111-54-0 LiN(Pr-i)<sub>2</sub>

SOL 109-99-9 THF

CON 1.5 hours, -80 deg C

STAGE(2)

RCT AH 914261-53-3

SOL 109-99-9 THF

CON SUBSTAGE(1) 3 hours, -80 deg C

SUBSTAGE(2) overnight, -80 deg C -> room temperature

STAGE(3)

RGT V 12125-02-9 NH<sub>4</sub>Cl

SOL 7732-18-5 Water

STAGE(4)

CAT 196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium salt (1:3)

SOL 108-88-3 PhMe

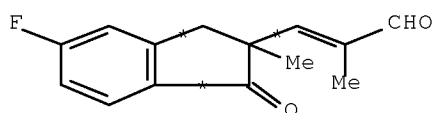
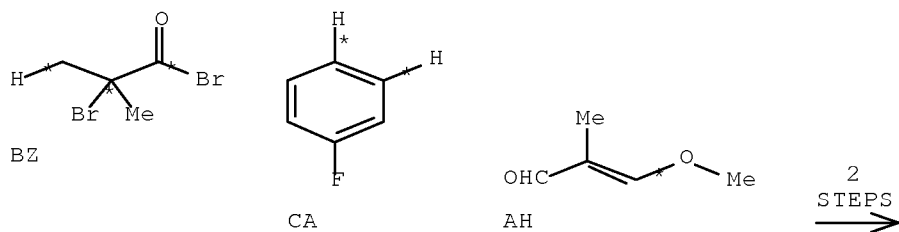
CON 1 hour, reflux

PRO AK 914261-54-4

RX(69) OF 153 COMPOSED OF RX(37), RX(11)

RX(69) BZ + CA + AH ==> AI

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AI  
YIELD 82%

RX(37) RCT BZ 20769-85-1, CA 462-06-6  
RGT CB 7446-70-0 AlCl3  
PRO AG 41201-58-5  
SOL 75-15-0 CS2

RX(11) RCT AG 41201-58-5

STAGE(1)

RGT Q 4111-54-0 LiN(Pr-i)2  
SOL 109-99-9 THF  
CON 1.5 hours, -80 deg C

STAGE(2)

RCT AH 914261-53-3  
SOL 109-99-9 THF  
CON SUBSTAGE(1) 3 hours, -80 deg C  
SUBSTAGE(2) overnight, -80 deg C -> room temperature

STAGE(3)

RGT V 12125-02-9 NH4Cl  
SOL 7732-18-5 Water

STAGE(4)

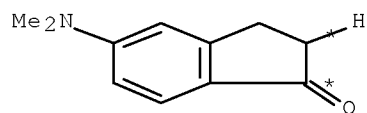
CAT 196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium salt (1:3)  
SOL 108-88-3 PhMe  
CON 1 hour, reflux

PRO AI 914261-70-4

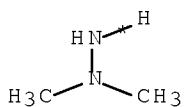
RX(73) OF 153 COMPOSED OF RX(3), RX(4), RX(12)

RX(73) G + K + O + AH ==> AK

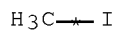
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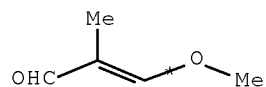
G



K

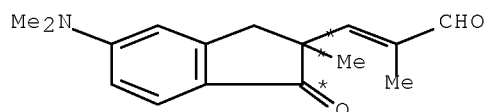


O



AH

3  
STEPS  
→



AK  
YIELD 80%

RX(3) RCT G 51981-67-0, K 57-14-7  
PRO L 914261-36-2  
CAT 104-15-4 TsOH  
SOL 108-88-3 PhMe  
NTE Dean-Stark trap used

RX(4) RCT L 914261-36-2, O 74-88-4

STAGE(1)

RGT Q 4111-54-0 LiN(Pr-i)2  
CON -40 deg C

STAGE(2)

RGT R 12408-02-5 H+

PRO P 914261-49-7

RX(12) RCT P 914261-49-7

STAGE(1)

RGT Q 4111-54-0 LiN(Pr-i)2  
SOL 109-99-9 THF  
CON 1.5 hours, -80 deg C

STAGE(2)

RCT AH 914261-53-3  
SOL 109-99-9 THF  
CON SUBSTAGE(1) 3 hours, -80 deg C  
SUBSTAGE(2) overnight, -80 deg C -> room temperature



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STAGE(3)

RGT V 12125-02-9 NH4Cl

SOL 7732-18-5 Water

STAGE(4)

CAT 196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium salt (1:3)

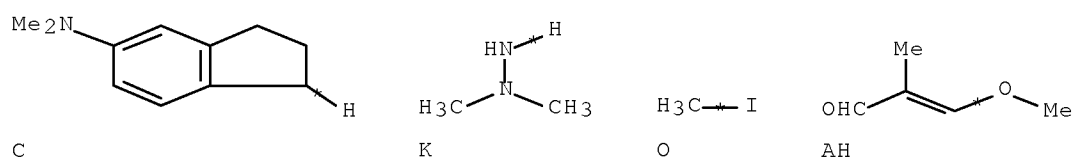
SOL 108-88-3 PhMe

CON 1 hour, reflux

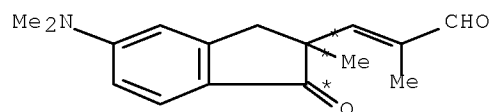
PRO AK 914261-54-4

RX(74) OF 153 COMPOSED OF RX(2), RX(3), RX(4), RX(12)

RX(74) C + K + O + AH ==> AK



4  
STEPS  
→



AK  
YIELD 80%

RX(2) RCT C 871886-03-2  
RGT H 84-58-2 DDQ  
PRO G 51981-67-0  
SOL 7732-18-5 Water, 109-99-9 THF  
CON 1 hour, room temperature

RX(3) RCT G 51981-67-0, K 57-14-7  
PRO L 914261-36-2  
CAT 104-15-4 TsOH  
SOL 108-88-3 PhMe  
NTE Dean-Stark trap used

RX(4) RCT L 914261-36-2, O 74-88-4

STAGE(1)

RGT Q 4111-54-0 LiN(Pr-i)<sub>2</sub>

CON -40 deg C

STAGE(2)

RGT R 12408-02-5 H<sup>+</sup>

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PRO P 914261-49-7

RX(12) RCT P 914261-49-7

STAGE(1)

RGT Q 4111-54-0 LiN(Pr-i)2

SOL 109-99-9 THF

CON 1.5 hours, -80 deg C

STAGE(2)

RCT AH 914261-53-3

SOL 109-99-9 THF

CON SUBSTAGE(1) 3 hours, -80 deg C

SUBSTAGE(2) overnight, -80 deg C -> room temperature

STAGE(3)

RGT V 12125-02-9 NH4Cl

SOL 7732-18-5 Water

STAGE(4)

CAT 196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium salt (1:3)

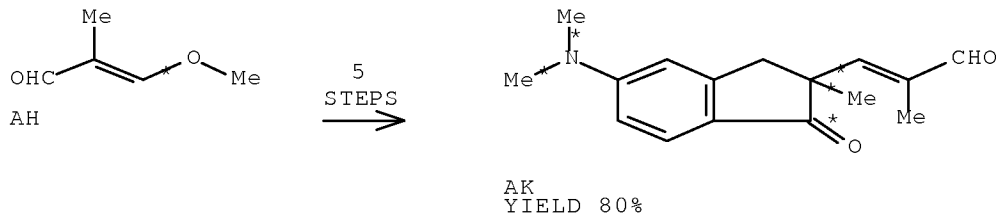
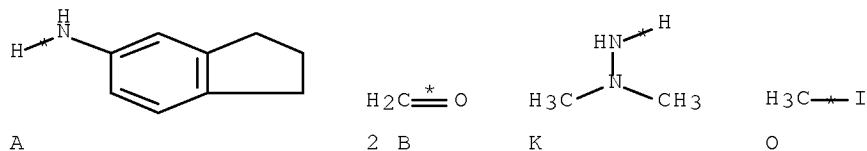
SOL 108-88-3 PhMe

CON 1 hour, reflux

PRO AK 914261-54-4

RX(119) OF 153 COMPOSED OF RX(1), RX(2), RX(3), RX(4), RX(12)

RX(119) A + 2 B + K + O + AH ==> AK



RX(1) RCT A 24425-40-9, B 50-00-0

STAGE(1)

RGT D 25895-60-7 NaBH3CN

SOL 75-05-8 MeCN

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CON 15 minutes, room temperature

STAGE(2)

RGT E 64-19-7 AcOH

CON neutralized

PRO C 871886-03-2

RX(2)

RCT C 871886-03-2

RGT H 84-58-2 DDQ

PRO G 51981-67-0

SOL 7732-18-5 Water, 109-99-9 THF

CON 1 hour, room temperature

RX(3)

RCT G 51981-67-0, K 57-14-7

PRO L 914261-36-2

CAT 104-15-4 TsOH

SOL 108-88-3 PhMe

NTE Dean-Stark trap used

RX(4)

RCT L 914261-36-2, O 74-88-4

STAGE(1)

RGT Q 4111-54-0 LiN(Pr-i)<sub>2</sub>

CON -40 deg C

STAGE(2)

RGT R 12408-02-5 H<sup>+</sup>

PRO P 914261-49-7

RX(12)

RCT P 914261-49-7

STAGE(1)

RGT Q 4111-54-0 LiN(Pr-i)<sub>2</sub>

SOL 109-99-9 THF

CON 1.5 hours, -80 deg C

STAGE(2)

RCT AH 914261-53-3

SOL 109-99-9 THF

CON SUBSTAGE(1) 3 hours, -80 deg C

SUBSTAGE(2) overnight, -80 deg C -> room temperature

STAGE(3)

RGT V 12125-02-9 NH<sub>4</sub>Cl

SOL 7732-18-5 Water

STAGE(4)

CAT 196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium salt (1:3)

SOL 108-88-3 PhMe

CON 1 hour, reflux

PRO AK 914261-54-4

L48 ANSWER 3 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 143:477858 CASREACT Full-text

TITLE: Preparation of substituted pyrido[3,2-b]indoles for

use in pharmaceutical compositions for the treatment of HIV-infection

INVENTOR(S): Kesteley, Bart Rudolf Romanie; Van De Vreken, Wim; Kindermans, Natalie Maria Francisca; Canard, Maxime Francis Jean-Marie Ghislain; Hertogs, Kurt; Bettens, Eva; De Vroey, Veronique Corine Paul; Jochmans, Dirk Edward Desire; Wigerinck, Piet Tom Bert Paul; Wang, Jing; Tahri, Abdellah; Surleraux, Dominique Louis Nestor Ghislain

PATENT ASSIGNEE(S): Tibotec Pharmaceuticals Ltd., Ire.

SOURCE: PCT Int. Appl., 92 pp.  
CODEN: PIXXD2

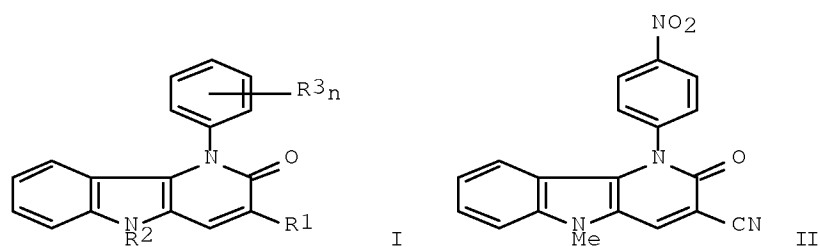
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

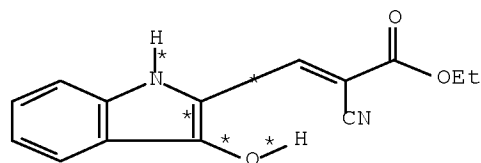
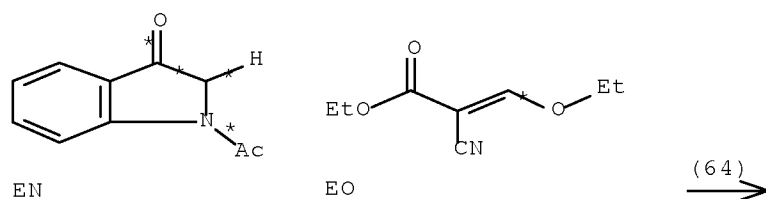
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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AU 2005244449	A1	20051124	AU 2005-244449	20050517
CA 2563601	A1	20051124	CA 2005-2563601	20050517
EP 1750708	A1	20070214	EP 2005-747916	20050517
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1953751	A	20070425	CN 2005-80015688	20050517
BR 2005011144	A	20071127	BR 2005-11144	20050517
JP 2007538053	T	20071227	JP 2007-517256	20050517
IN 2006DN06106	A	20070831	IN 2006-DN6106	20061019
US 20070249655	A1	20071025	US 2006-569111	20061114
MX 2006PA13316	A	20070202	MX 2006-PA13316	20061116
KR 2007011588	A	20070124	KR 2006-725921	20061208
PRIORITY APPLN. INFO.:			EP 2004-102173	20040517
			US 2004-102173	20040517
			WO 2005-EP52266	20050517
OTHER SOURCE(S):			MARPAT 143:477858	
GI				



AB Pyrido[3,2-b]indoles, such as I [R1 = H, CN, halogen, alkylcarbonyl, etc.; R2 = H, (hetero)alkyl, alkenyl, etc.; R3 = NO<sub>2</sub>, CN, OH, (un)substituted amino, etc.; n = 1-3; and their N-oxides, salts, stereoisomers, racemic mixts., prodrugs, esters or metabolites thereof], were prepared for therapeutic use and anti-HIV agents. Thus, pyrido[3,2-b]indole II was prepared via a five step synthetic scheme starting from the reaction of 1-acetyl-3-hydroxyindole with 4-nitroaniline. The prepared pyrido[3,2-b]indoles were tested for inhibition of HIV reverse transcriptase, for metabolism using human liver microsomal fractions and for anti-HIV activity. Thus, I and their pharmaceutical compns. are useful for the treatment of retroviral infections such as HIV infection, in particular, in the treatment of infections with multi-drug resistant retroviruses.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(64) OF 302 EN + EO ==> CN...



CN  
YIELD 92%

RX(64) RCT EN 16800-68-3

## STAGE(1)

RGT DW 7646-69-7 NaH  
 SOL 109-99-9 THF  
 CON 30 minutes, -78 deg C

## STAGE(2)

RCT EO 94-05-3  
 CON SUBSTAGE(1) 15 minutes, -78 deg C  
 SUBSTAGE(2) 1 hour, -78 deg C  
 SUBSTAGE(3) overnight, -78 deg C -> room temperature

## STAGE(3)

RGT L 7647-01-0 HCl  
 SOL 7732-18-5 Water  
 CON cooled, pH 1

PRO CN 136429-63-5

L48 ANSWER 4 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 142:298286 CASREACT Full-text

TITLE: Preparation of tricyclic nucleosides or nucleotides as  
 antiviral and antitumor therapeutic agents

INVENTOR(S): Cook, Phillip Dan; Ewing, Gregory; Jin, Yi; Lambert,  
 John; Prhavo, Marija; Rajappan, Vasanthakumar;  
 Rajwanshi, Vivek K.; Sakthivel, Kandasamy

PATENT ASSIGNEE(S): Biota, Inc., USA

SOURCE: PCT Int. Appl., 106 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005021568	A2	20050310	WO 2004-US27819	20040827
WO 2005021568	A3	20050421		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2004269026	A1	20050310	AU 2004-269026	20040827
CA 2537114	A1	20050310	CA 2004-2537114	20040827
EP 1660511	A2	20060531	EP 2004-782317	20040827
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK			
BR 2004014019	A	20061024	BR 2004-14019	20040827
CN 1863813	A	20061115	CN 2004-80029262	20040827
JP 2007504152	T	20070301	JP 2006-524865	20040827
MX 2006PA02198	A	20070814	MX 2006-PA2198	20060224
NO 2006000979	A	20060502	NO 2006-979	20060228
IN 2006KN00570	A	20070706	IN 2006-KN570	20060309

10/569486

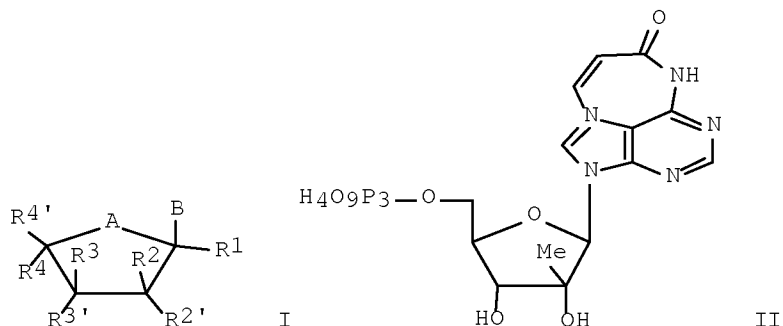
US 20080200423	A1	20080821	US 2006-568917	20061129
US 20070135363	A1	20070614	US 2007-674954	20070214
US 7268119	B2	20070911		

PRIORITY APPLN. INFO.:

US 2003-498425P	20030827
WO 2004-US27819	20040827
US 2006-568917	20061129

OTHER SOURCE(S): MARPAT 142:298286

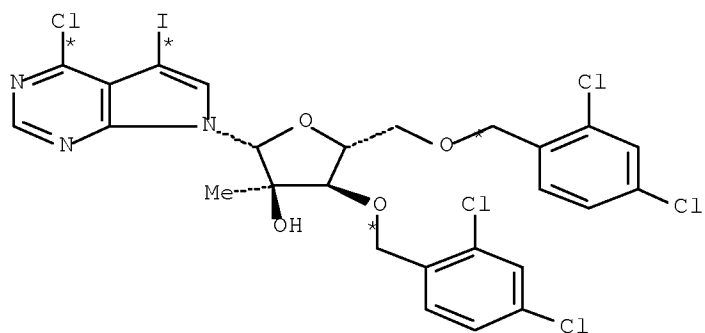
GI



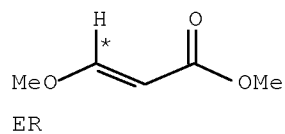
AB Nucleosides and nucleotides containing a tricyclic base portion I, wherein A is O, S, CH2, NH, CHF, CF2; R1, R2, R2', R3, R3', R4 are independently H, F, Cl, iodo, Br, OH, SH, NH2, NHOH, NHNH2, N3, COOH, CN, CONH2, CSNH2, COOR, R, OR, SR, SSR, NHR, NR2; R4' is L-R5; L is O, S, NH, NR, CY2S, CY2NH, CY2, CY2CY2, CY2OCY2, CY2SCY2, CY2NHCY2; Y is H, F, Cl, Br, alkyl, alkenyl, alkynyl, R4' is OH, monophosphate, diphosphate, triphosphate; B is substituted tricyclic nucleobase derivs.; R is alkyl, alkenyl, alkynyl, aryl, acyl, aralkyl; thereof are useful for treating infectious diseases and proliferative disorders, such as viral infections or cancer resp. Thus, nucleotide II was prepared and tested in vitro as polymerase inhibitor, antiviral, and antitumor therapeutic agent. Title compds. were typically cytotoxic in the range of 30 to > 100  $\mu$ M. II showed inhibitory of NS5B in the range of 100 to >1000 nM. Selected examples displayed IC50 values in the range of to 100 nM.

RX(305) OF 542 COMPOSED OF RX(56), RX(57), RX(62)  
 RX(305) CD + ER ==> ES

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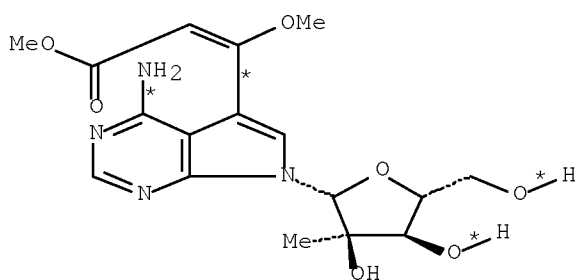


CD



ER

3  
STEPS  
→



ES  
YIELD 45%

RX(56) RCT CD 847551-25-1

STAGE(1)

RGT AV 10294-34-5 BC13

SOL 75-09-2 CH2Cl2

CON SUBSTAGE(1) 2.5 hours, -78 deg C

SUBSTAGE(2) 3 hours, -30 - -20 deg C

STAGE(2)

RGT N 67-56-1 MeOH

SOL 75-09-2 CH2Cl2

CON SUBSTAGE(2) 0.5 hours, -15 deg C

STAGE(3)

RGT M 7664-41-7 NH3

SOL 7732-18-5 Water

CON SUBSTAGE(1) 0 deg C, neutralized



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SUBSTAGE(2) 0.25 hours, room temperature

PRO EJ 847551-48-8

RX(57) RCT EJ 847551-48-8  
RGT M 7664-41-7 NH3  
PRO EK 847551-49-9  
SOL 7664-41-7 NH3  
CON SUBSTAGE(1) overnight, 85 deg C  
SUBSTAGE(2) cooled  
NTE thermal, chemoselective, autoclave used

RX(62) RCT EK 847551-49-9, ER 5788-17-0

STAGE(1)

RGT Q 121-44-8 Et3N  
CAT 14221-01-3 Pd(PPh3)4, 7681-65-4 CuI  
SOL 68-12-2 DMF  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 24 hours, 70 deg C  
SUBSTAGE(3) 70 deg C -> room temperature

STAGE(2)

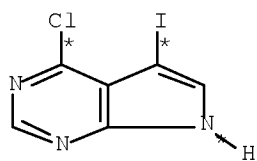
RGT R 11114-15-1 DOWEX 50W  
SOL 67-56-1 MeOH, 75-09-2 CH2Cl2  
CON 45 minutes, room temperature

PRO ES 847551-54-6

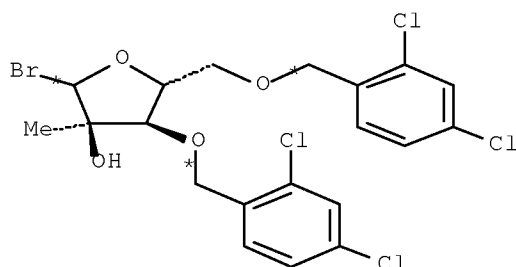
NTE Dowex 1x2-100 Bicarb form of reagent used in stage 2

RX(309) OF 542 COMPOSED OF RX(30), RX(56), RX(57), RX(62)

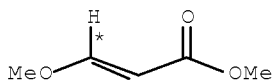
RX(309) CC + AG + ER ==> ES



CC



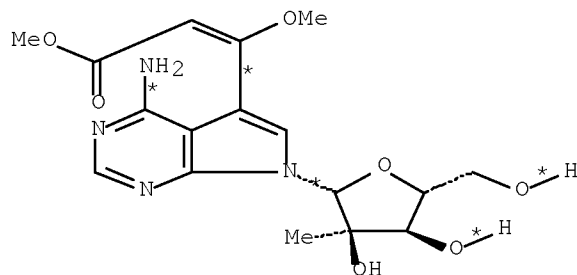
AG



ER

4  
STEPS  
→

10/569486



ES  
YIELD 45%

RX(30) RCT CC 123148-78-7

STAGE(1)

RGT BO 7646-69-7 NaH  
SOL 75-05-8 MeCN  
CON 4 hours, room temperature

STAGE(2)

RCT AG 847551-03-5  
SOL 75-05-8 MeCN  
CON 24 hours, room temperature

STAGE(3)

RGT J 7732-18-5 Water  
CON room temperature

PRO CD 847551-25-1  
NTE stereoselective

RX(56) RCT CD 847551-25-1

STAGE(1)

RGT AV 10294-34-5 BC13  
SOL 75-09-2 CH2Cl2  
CON SUBSTAGE(1) 2.5 hours, -78 deg C  
SUBSTAGE(2) 3 hours, -30 - -20 deg C

STAGE(2)

RGT N 67-56-1 MeOH  
SOL 75-09-2 CH2Cl2  
CON SUBSTAGE(2) 0.5 hours, -15 deg C

STAGE(3)

RGT M 7664-41-7 NH3  
SOL 7732-18-5 Water  
CON SUBSTAGE(1) 0 deg C, neutralized  
SUBSTAGE(2) 0.25 hours, room temperature

PRO EJ 847551-48-8

RX(57) RCT EJ 847551-48-8  
RGT M 7664-41-7 NH3

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PRO EK 847551-49-9  
SOL 7664-41-7 NH3  
CON SUBSTAGE(1) overnight, 85 deg C  
SUBSTAGE(2) cooled  
NTE thermal, chemoselective, autoclave used

RX(62) RCT EK 847551-49-9, ER 5788-17-0

STAGE(1)

RGT Q 121-44-8 Et3N  
CAT 14221-01-3 Pd(PPh3)4, 7681-65-4 CuI  
SOL 68-12-2 DMF  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 24 hours, 70 deg C  
SUBSTAGE(3) 70 deg C -> room temperature

STAGE(2)

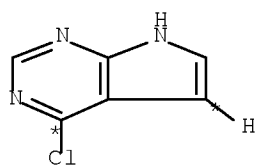
RGT R 11114-15-1 DOWEX 50W  
SOL 67-56-1 MeOH, 75-09-2 CH2Cl2  
CON 45 minutes, room temperature

PRO ES 847551-54-6

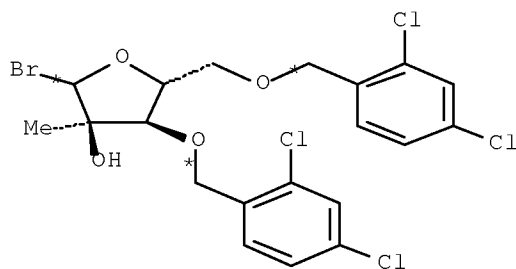
NTE Dowex 1x2-100 Bicarb form of reagent used in stage 2

RX(409) OF 542 COMPOSED OF RX(29), RX(30), RX(56), RX(57), RX(62)

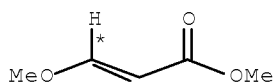
RX(409) X + AG + ER ==> ES



X



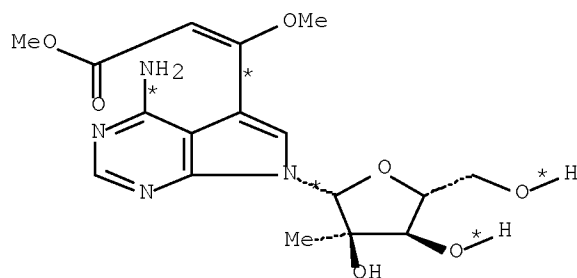
AG



ER

5  
STEPS  
→

10/569486



ES  
YIELD 45%

RX(29) RCT X 3680-69-1  
RGT C 516-12-1 Iodosuccinimide  
PRO CC 123148-78-7  
SOL 109-99-9 THF  
CON 4 hours, room temperature  
NTE regioselective

RX(30) RCT CC 123148-78-7

STAGE(1)  
RGT BO 7646-69-7 NaH  
SOL 75-05-8 MeCN  
CON 4 hours, room temperature

STAGE(2)  
RCT AG 847551-03-5  
SOL 75-05-8 MeCN  
CON 24 hours, room temperature

STAGE(3)  
RGT J 7732-18-5 Water  
CON room temperature

PRO CD 847551-25-1  
NTE stereoselective

RX(56) RCT CD 847551-25-1

STAGE(1)  
RGT AV 10294-34-5 BC13  
SOL 75-09-2 CH2Cl2  
CON SUBSTAGE(1) 2.5 hours, -78 deg C  
SUBSTAGE(2) 3 hours, -30 - -20 deg C

STAGE(2)  
RGT N 67-56-1 MeOH  
SOL 75-09-2 CH2Cl2  
CON SUBSTAGE(2) 0.5 hours, -15 deg C

STAGE(3)  
RGT M 7664-41-7 NH3  
SOL 7732-18-5 Water  
CON SUBSTAGE(1) 0 deg C, neutralized

SUBSTAGE(2) 0.25 hours, room temperature

PRO EJ 847551-48-8

RX(57) RCT EJ 847551-48-8  
 RGT M 7664-41-7 NH3  
 PRO EK 847551-49-9  
 SOL 7664-41-7 NH3  
 CON SUBSTAGE(1) overnight, 85 deg C  
 SUBSTAGE(2) cooled  
 NTE thermal, chemoselective, autoclave used

RX(62) RCT EK 847551-49-9, ER 5788-17-0

STAGE(1)

RGT Q 121-44-8 Et3N  
 CAT 14221-01-3 Pd(PPh3)4, 7681-65-4 CuI  
 SOL 68-12-2 DMF  
 CON SUBSTAGE(1) room temperature  
 SUBSTAGE(2) 24 hours, 70 deg C  
 SUBSTAGE(3) 70 deg C -> room temperature

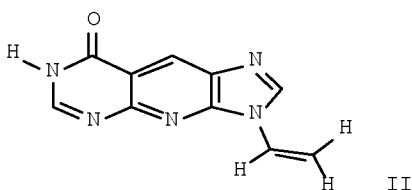
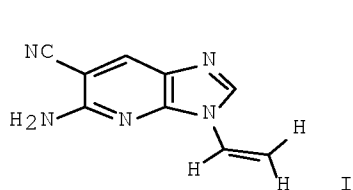
STAGE(2)

RGT R 11114-15-1 DOWEX 50W  
 SOL 67-56-1 MeOH, 75-09-2 CH2Cl2  
 CON 45 minutes, room temperature

PRO ES 847551-54-6

NTE Dowex 1x2-100 Bicarb form of reagent used in stage 2

L48 ANSWER 5 OF 16 CASREACT COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 142:56252 CASREACT Full-text  
 TITLE: Routes to N-vinyl-nitroimidazoles and  
 N-vinyl-deazapurines  
 AUTHOR(S): Clayton, Russell; Ramsden, Christopher A.  
 CORPORATE SOURCE: Lennard-Jones Laboratories, School of Chemistry and  
 Physics, Keele University, Keele, ST5 5BG, UK  
 SOURCE: Journal of Heterocyclic Chemistry (2004), 41(5),  
 701-705  
 CODEN: JHTCAD; ISSN: 0022-152X  
 PUBLISHER: HeteroCorporation  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



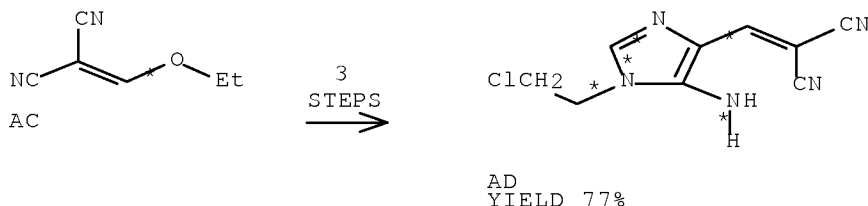
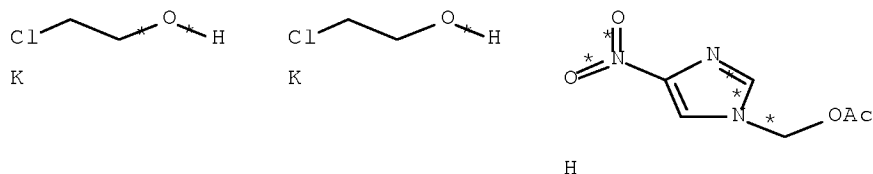
10/569486

AB The prepn. of 4- and 5-nitro-1-vinylimidazole are described. Selective reduction of the nitro group using Fe/dil.HCl was achieved for the 4-nitro derivative but this was not effective when ethoxymethylenemalononitrile was used to trap the amine. For 5-nitroimidazole studies the N-vinyl substituent was kept masked as a 2-chloroethyl group, which remained unchanged during catalytic reduction of the nitro function, and it was revealed by HCl elimination at a later stage. The 1-deazapurine I and the tricyclic derivative II have been prepared

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(25) OF 42 COMPOSED OF RX(3), RX(4), RX(8)

RX(25) 2 K + H + AC ==> AD



RX(3) RCT K 107-07-3  
RGT M 7791-25-5 SO2Cl2  
PRO L 5411-48-3  
SOL 75-09-2 CH2Cl2  
CON 2 hours, 0 deg C

RX(4) RCT H 5709-48-8, L 5411-48-3

STAGE(1)  
CON 2 hours, 100 deg C

STAGE(2)  
RGT D 7664-93-9 H2SO4  
SOL 7732-18-5 Water  
CON SUBSTAGE(1) 2 hours, reflux  
SUBSTAGE(2) cooled

STAGE(3)  
RGT P 1310-73-2 NaOH  
SOL 7732-18-5 Water  
CON 0 deg C, pH 11

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PRO O 13182-80-4  
NTE no solvent in stage 1

RX(8) RCT O 13182-80-4

STAGE(1)

RGT W 1333-74-0 H2  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane  
CON room temperature, 1 atm

STAGE(2)

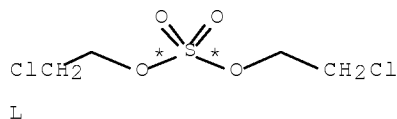
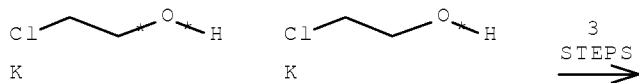
RCT AC 123-06-8  
SOL 123-91-1 Dioxane  
CON overnight, room temperature

PRO AD 810660-39-0

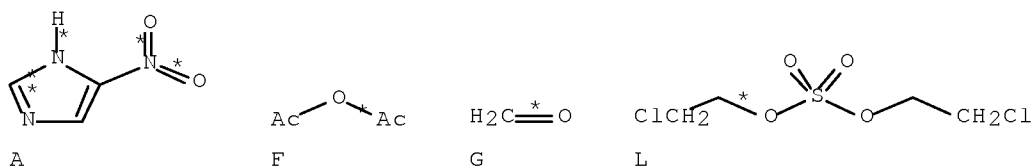
RX(34) OF 42 COMPOSED OF REACTION SEQUENCE RX(3), RX(4), RX(8)  
AND REACTION SEQUENCE RX(2), RX(4), RX(8)

...2 K ==> L...

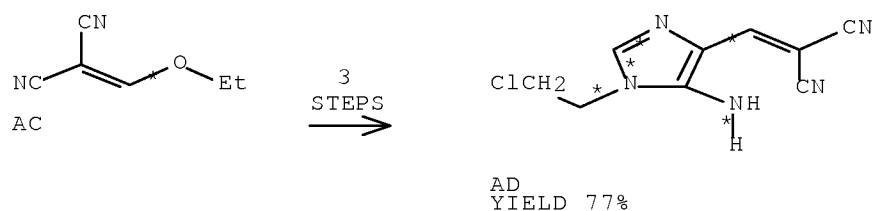
... A + F + G + L + AC ==> AD



START NEXT REACTION SEQUENCE



10/569486



RX(3) RCT K 107-07-3  
RGT M 7791-25-5 SO2Cl2  
PRO L 5411-48-3  
SOL 75-09-2 CH2Cl2  
CON 2 hours, 0 deg C

RX(2) RCT A 3034-38-6, F 108-24-7, G 50-00-0  
PRO H 5709-48-8  
CAT 127-09-3 AcONa  
SOL 108-88-3 PhMe  
CON 90 hours, 100 deg C  
NTE paraformaldehyde used

RX(4) RCT H 5709-48-8, L 5411-48-3

STAGE(1)  
CON 2 hours, 100 deg C

STAGE(2)  
RGT D 7664-93-9 H2SO4  
SOL 7732-18-5 Water  
CON SUBSTAGE(1) 2 hours, reflux  
SUBSTAGE(2) cooled

STAGE(3)  
RGT P 1310-73-2 NaOH  
SOL 7732-18-5 Water  
CON 0 deg C, pH 11

PRO O 13182-80-4  
NTE no solvent in stage 1

RX(8) RCT O 13182-80-4

STAGE(1)  
RGT W 1333-74-0 H2  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane  
CON room temperature, 1 atm

STAGE(2)  
RCT AC 123-06-8  
SOL 123-91-1 Dioxane  
CON overnight, room temperature

PRO AD 810660-39-0



10/569486

L48 ANSWER 6 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 139:85383 CASREACT [Full-text](#)

TITLE: Preparation of pyridoquinoxaline derivatives as antiviral agents

INVENTOR(S): Strohbach, Joseph W.; Tanis, Steven P.; Moon, Malcolm W.; Perrault, William R.

PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

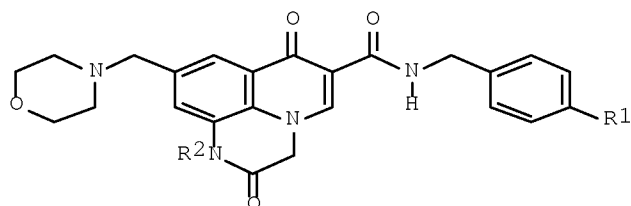
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053972	A1	20030703	WO 2002-US37614	20021219
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2473862	A1	20030703	CA 2002-2473862	20021219
AU 2002352882	A1	20030709	AU 2002-352882	20021219
US 20030130255	A1	20030710	US 2002-325248	20021219
US 6686356	B2	20040203		
EP 1456208	A1	20040915	EP 2002-789842	20021219
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
BR 2002015067	A	20041109	BR 2002-15067	20021219
JP 2005516957	T	20050609	JP 2003-554688	20021219
US 20040106596	A1	20040603	US 2003-721119	20031125
MX 2004PA06030	A	20040927	MX 2004-PA6030	20040618
PRIORITY APPLN. INFO.:			US 2001-342874P	20011220
			US 2002-325248	20021219
			WO 2002-US37614	20021219

OTHER SOURCE(S): MARPAT 139:85383

GI

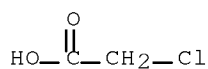


I

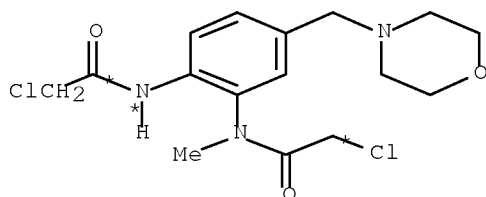
AB The present invention provides a synthesis of pyridoquinoxaline derivs. I (R1 = F, Cl, Br, cyano, NO2, R2 = alkyl, substituted alkyl, arylalkyl, etc.) to be used as antiviral agents. Thus, I (R1 = Cl, R2 = Me) was prepared by two methods, both starting from 3-fluoro-4-nitrotoluene (II). Thus, II was brominated and reacted with morpholine to give 4-(3-fluoro-4-nitrobenzyl)morpholine, which was converted to N-methyl-5-(morpholin-4-ylmethyl)-2-nitroaniline. The latter compound was then converted to I (R1 = Cl, R2 = Me) in 4 steps. The compds. are intended to be used as antiviral agents to treat human herpesviruses, human simplex viruses, and cytomegalovirus. They can be administered orally, parenterally, or topically. These compds. are also designed to inhibit DNA polymerase and treat atherosclerosis and restenosis.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

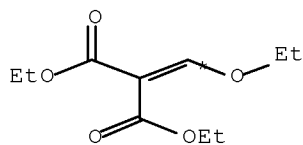
RX(12) OF 63 ...AG + O ==> AH...



AG: CM 1

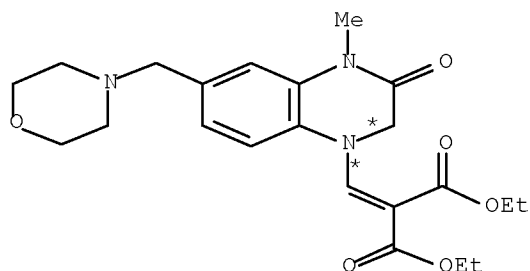


AG: CM 2



O

(12) →



AH

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RX(12) RCT AG 552884-01-2

STAGE(1)

RGT AI 1310-73-2 NaOH

SOL 7732-18-5 Water, 109-99-9 THF

CON SUBSTAGE(1) 13 - 17 deg C

SUBSTAGE(2) 20 minutes

STAGE(2)

RGT AJ 12125-02-9 NH4Cl

SOL 7732-18-5 Water, 108-88-3 PhMe

STAGE(3)

RCT O 87-13-8

CON SUBSTAGE(2) 123 deg C

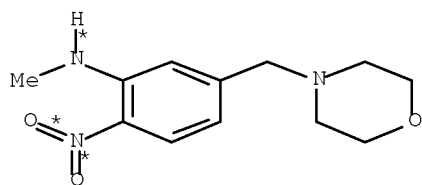
SUBSTAGE(3) 3 hours, 122 - 125 deg C

PRO AH 552884-02-3

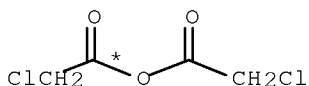
NTE Isopar-H present in last stage

RX(24) OF 63 COMPOSED OF RX(11), RX(12)

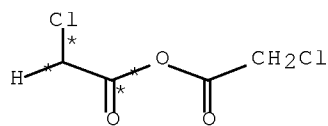
RX(24) AC + 3 AF + O ==> AH



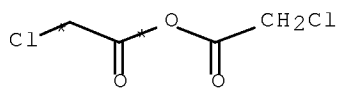
AC



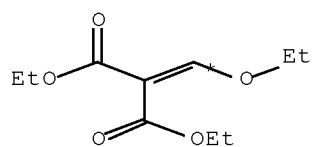
AF



AF



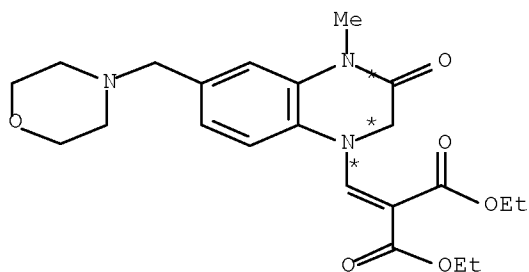
AF



O

2  
STEPS  
→

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AH

RX(11) RCT AC 552883-99-5

STAGE(1)

RGT L 1333-74-0 H2  
CAT 7440-05-3 Pd  
SOL 109-99-9 THF  
CON 1 hour, 14 deg C

STAGE(2)

RCT AF 541-88-8  
SOL 109-99-9 THF  
CON SUBSTAGE(1) 10 deg C  
SUBSTAGE(2) 30 minutes, 8 - 11 deg C  
SUBSTAGE(3) 30 minutes

PRO AG 552884-01-2

RX(12) RCT AG 552884-01-2

STAGE(1)

RGT AI 1310-73-2 NaOH  
SOL 7732-18-5 Water, 109-99-9 THF  
CON SUBSTAGE(1) 13 - 17 deg C  
SUBSTAGE(2) 20 minutes

STAGE(2)

RGT AJ 12125-02-9 NH4Cl  
SOL 7732-18-5 Water, 108-88-3 PhMe

STAGE(3)

RCT O 87-13-8  
CON SUBSTAGE(2) 123 deg C  
SUBSTAGE(3) 3 hours, 122 - 125 deg C

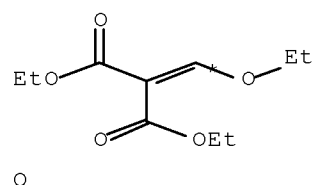
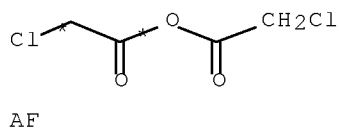
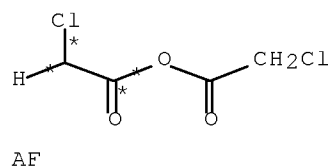
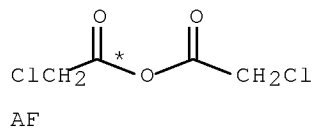
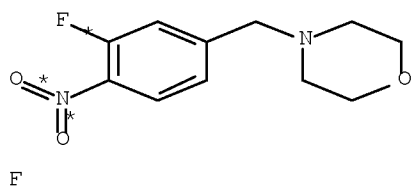
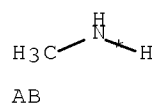
PRO AH 552884-02-3

NTE Isopar-H present in last stage

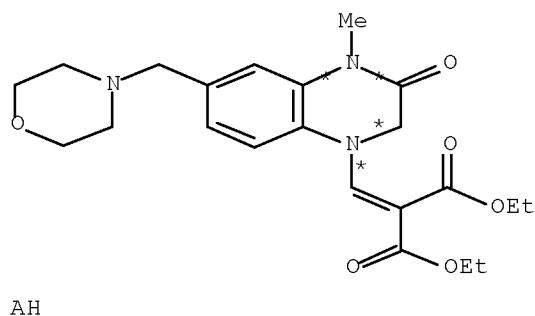
RX(42) OF 63 COMPOSED OF RX(10), RX(11), RX(12)

RX(42) AB + F + 3 AF + O ==> AH

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3  
STEPS  
→



RX(10) RCT AB 74-89-5, F 552883-91-7

STAGE(1)

SOL 7732-18-5 Water, 67-68-5 DMSO

CON SUBSTAGE(2) 30 minutes

SUBSTAGE(3) 5 minutes, 47 deg C

SUBSTAGE(4) <51 deg C

SUBSTAGE(5) 45 minutes, 50 deg C

STAGE(2)

SOL 7732-18-5 Water

PRO AC 552883-99-5

RX(11) RCT AC 552883-99-5

STAGE(1)

RGT L 1333-74-0 H2

CAT 7440-05-3 Pd

SOL 109-99-9 THF

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CON 1 hour, 14 deg C

STAGE(2)

RCT AF 541-88-8

SOL 109-99-9 THF

CON SUBSTAGE(1) 10 deg C

SUBSTAGE(2) 30 minutes, 8 - 11 deg C

SUBSTAGE(3) 30 minutes

PRO AG 552884-01-2

RX(12) RCT AG 552884-01-2

STAGE(1)

RGT AI 1310-73-2 NaOH

SOL 7732-18-5 Water, 109-99-9 THF

CON SUBSTAGE(1) 13 - 17 deg C

SUBSTAGE(2) 20 minutes

STAGE(2)

RGT AJ 12125-02-9 NH4Cl

SOL 7732-18-5 Water, 108-88-3 PhMe

STAGE(3)

RCT O 87-13-8

CON SUBSTAGE(2) 123 deg C

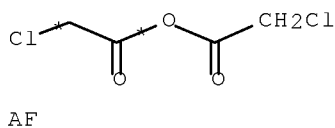
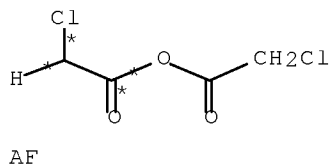
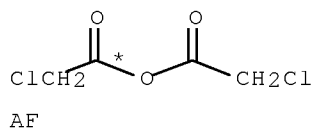
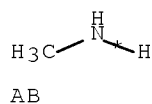
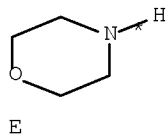
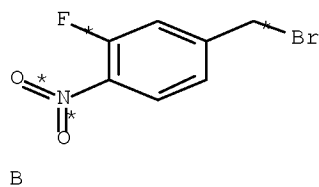
SUBSTAGE(3) 3 hours, 122 - 125 deg C

PRO AH 552884-02-3

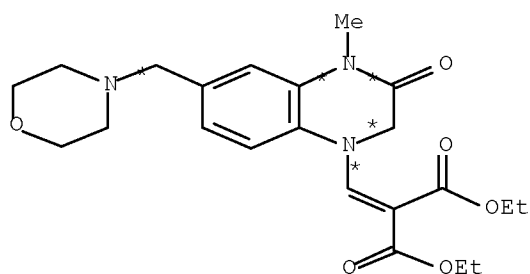
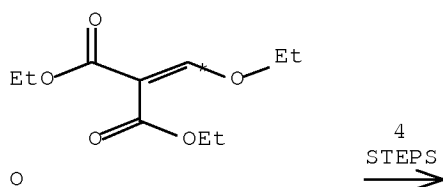
NTE Isopar-H present in last stage

RX(43) OF 63 COMPOSED OF RX(2), RX(10), RX(11), RX(12)

RX(43) E + E + AB + 3 AF + O ==> AH



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AH

RX(2) RCT B 131858-37-2, E 110-91-8  
 PRO F 552883-91-7  
 SOL 109-99-9 THF  
 CON SUBSTAGE(1) room temperature  
 SUBSTAGE(2) 1 hour, room temperature

RX(10) RCT AB 74-89-5, F 552883-91-7

STAGE(1)

SOL 7732-18-5 Water, 67-68-5 DMSO

CON SUBSTAGE(2) 30 minutes

SUBSTAGE(3) 5 minutes, 47 deg C

SUBSTAGE(4) <51 deg C

SUBSTAGE(5) 45 minutes, 50 deg C

STAGE(2)

SOL 7732-18-5 Water

PRO AC 552883-99-5

RX(11) RCT AC 552883-99-5

STAGE(1)

RGT L 1333-74-0 H2

CAT 7440-05-3 Pd

SOL 109-99-9 THF

CON 1 hour, 14 deg C

STAGE(2)

RCT AF 541-88-8

SOL 109-99-9 THF

CON SUBSTAGE(1) 10 deg C

SUBSTAGE(2) 30 minutes, 8 - 11 deg C

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SUBSTAGE(3) 30 minutes

PRO AG 552884-01-2

RX(12) RCT AG 552884-01-2

STAGE(1)

RGT AI 1310-73-2 NaOH

SOL 7732-18-5 Water, 109-99-9 THF

CON SUBSTAGE(1) 13 - 17 deg C

SUBSTAGE(2) 20 minutes

STAGE(2)

RGT AJ 12125-02-9 NH4Cl

SOL 7732-18-5 Water, 108-88-3 PhMe

STAGE(3)

RCT O 87-13-8

CON SUBSTAGE(2) 123 deg C

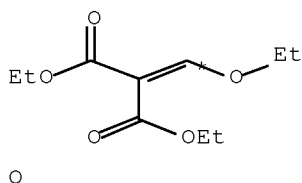
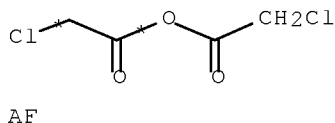
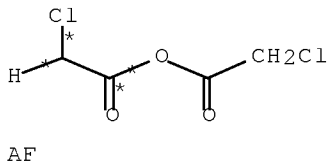
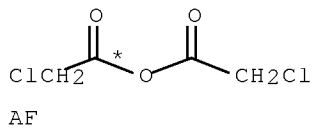
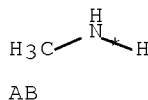
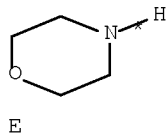
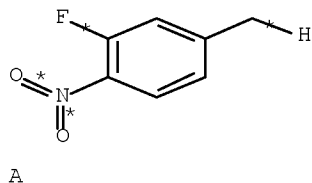
SUBSTAGE(3) 3 hours, 122 - 125 deg C

PRO AH 552884-02-3

NTE Isopar-H present in last stage

RX(47) OF 63 COMPOSED OF RX(1), RX(2), RX(10), RX(11), RX(12)

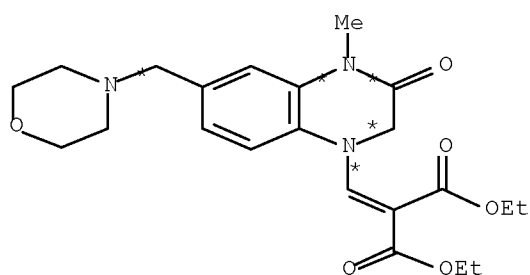
RX(47) A + E + AB + 3 AF + O ==> AH



5  
STEPS  
→



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AH

RX(1) RCT A 446-34-4  
RGT C 128-08-5 Bromosuccinimide  
PRO B 131858-37-2  
SOL 107-06-2 ClCH<sub>2</sub>CH<sub>2</sub>Cl  
CON SUBSTAGE(1) 1 hour, 0 - 25 deg C  
SUBSTAGE(3) 15 minutes  
NTE photochem.

RX(2) RCT B 131858-37-2, E 110-91-8  
PRO F 552883-91-7  
SOL 109-99-9 THF  
CON SUBSTAGE(1) room temperature  
SUBSTAGE(2) 1 hour, room temperature

RX(10) RCT AB 74-89-5, F 552883-91-7

STAGE(1)  
SOL 7732-18-5 Water, 67-68-5 DMSO  
CON SUBSTAGE(2) 30 minutes  
SUBSTAGE(3) 5 minutes, 47 deg C  
SUBSTAGE(4) <51 deg C  
SUBSTAGE(5) 45 minutes, 50 deg C

STAGE(2)  
SOL 7732-18-5 Water

PRO AC 552883-99-5

RX(11) RCT AC 552883-99-5

STAGE(1)  
RGT L 1333-74-0 H<sub>2</sub>  
CAT 7440-05-3 Pd  
SOL 109-99-9 THF  
CON 1 hour, 14 deg C

STAGE(2)  
RCT AF 541-88-8  
SOL 109-99-9 THF  
CON SUBSTAGE(1) 10 deg C  
SUBSTAGE(2) 30 minutes, 8 - 11 deg C

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SUBSTAGE(3) 30 minutes

PRO AG 552884-01-2

RX(12) RCT AG 552884-01-2

STAGE(1)

RGT AI 1310-73-2 NaOH  
SOL 7732-18-5 Water, 109-99-9 THF  
CON SUBSTAGE(1) 13 - 17 deg C  
SUBSTAGE(2) 20 minutes

STAGE(2)

RGT AJ ~~12125-02-9~~ NH4Cl  
SOL 7732-18-5 Water, 108-88-3 PhMe

STAGE(3)

RCT O ~~87-13-8~~  
CON SUBSTAGE(2) 123 deg C  
SUBSTAGE(3) 3 hours, 122 - 125 deg C

PRO AH 552884-02-3

NTE Isopar-H present in last stage

L48 ANSWER 7 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 139:52960 CASREACT Full-text

TITLE: Synthesis and antiinflammatory activity of novel  
indazolones

AUTHOR(S): Abouzid, Khaled A. M.; El-Abhar, H. S.

CORPORATE SOURCE: Pharmaceutical Chemistry Department, Faculty of  
Pharmacy, Ain-Shams University, Cairo, 11566, Egypt

SOURCE: Archives of Pharmacal Research (2003), 26(1), 1-8  
CODEN: APHRDQ; ISSN: 0253-6269

PUBLISHER: Pharmaceutical Society of Korea

DOCUMENT TYPE: Journal

LANGUAGE: English

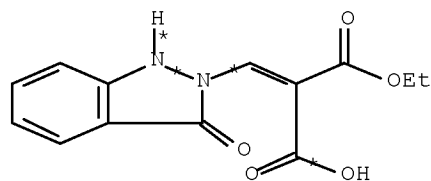
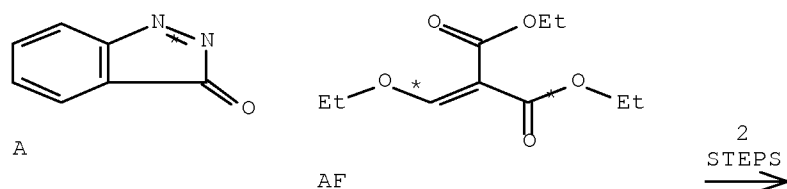
AB In this study, a series of new N2-substituted 1,2-dihydro-3H-indazol-3-ones as well as their condensed pyrazolo, pyridazino derivs. such as pyridazino[1,2-a]indazole-6,9,11-triones and 3,9-dioxo-3H,9H-pyrazolo[1,2-a]indazole were synthesized. The antiinflammatory activity of some synthesized compds. was determined by carrageenan-induced rat paw edema technique using diclofenac as reference drug. The pharmacol. data showed that most of the tested compds. exhibited a significant long lasting antiinflammatory activity, which in the case of  $\gamma$ ,3-dioxo- $\alpha$ -[(trifluoroacetyl)amino]-2H-Indazole-2-butanoic acid was superior to that of diclofenac.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(26) OF 35 COMPOSED OF RX(17), RX(18)

RX(26) A + AF ==> AJ

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AJ  
YIELD 37%

RX(17)      RCT    A 5686-93-1, AF 87-13-8  
               PRO    AI 545444-13-1  
               SOL    60-29-7 Et2O  
               CON    6 hours, 170 deg C

RX(18)      RCT    AI 545444-13-1

STAGE(1)

RGT   AK 1310-73-2 NaOH  
 SOL   7732-18-5 Water  
 CON   2 hours, room temperature

STAGE(2)

RGT   AL 7647-01-0 HCl  
 SOL   7732-18-5 Water

PRO   AJ 545444-14-2

L48   ANSWER 8 OF 16   CASREACT   COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:      135:210953   CASREACT   Full-text

TITLE:                      A convenient synthesis of 3,4-difunctionalized  
                                      $\delta$ -carboline

AUTHOR(S):                Papamicael, C.; Queguiner, G.; Bourguignon, J.; Dupas,  
                                     G.

CORPORATE SOURCE:      Laboratoire de Chimie Organique Fine et  
                                     Heterocyclique, UPRESA 6014, INSA-IRCOF,  
                                     Mont-Saint-Aignan, 76131, Fr.

SOURCE:                    Tetrahedron (2001), 57(25), 5385-5391  
                                     CODEN: TETRAB; ISSN: 0040-4020

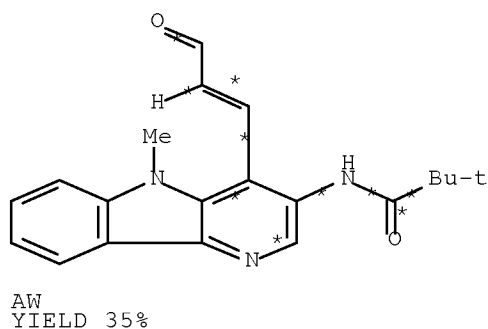
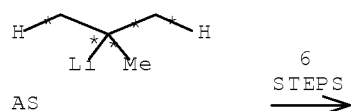
PUBLISHER:                Elsevier Science Ltd.

DOCUMENT TYPE:        Journal

LANGUAGE:                English

AB An efficient and direct preparation of functionalized  $\delta$ -carbolines, via a ring closure reaction between the appropriate indole amine and a masked 1,3-dicarbonyl compound is described. This method afforded new 3-substituted  $\delta$ -carbolines and these products were subjected to ortho-lithiation expts. Various 3,4-disubstituted  $\delta$ -carbolines were obtained in acceptable yields.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

$$\text{RX (89)} \quad \text{A} + \text{B} + \text{Y} + \text{AS} \implies \text{AW}$$


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```
RX(3)      RCT   C 358332-93-1

            STAGE(1)
              RGT   K 1310-73-2 NaOH, L 7722-84-1 H2O2
              SOL   64-17-5 EtOH, 7732-18-5 Water

            STAGE(2)
              RGT   M 7664-93-9 H2SO4
              SOL   7732-18-5 Water

            PRO   J 358332-94-2

RX(4)      RCT   J 358332-94-2

            STAGE(1)
              RGT   K 1310-73-2 NaOH
              SOL   64-17-5 EtOH

            STAGE(2)
              RGT   D 7647-01-0 HCl
              SOL   7732-18-5 Water

            PRO   O 358332-95-3

RX(7)      RCT   O 358332-95-3, Y 75-65-0
            RGT   AA 26386-88-9 (PhO)2P(O)N3, AB 121-44-8 Et3N
            PRO   Z 358332-98-6
            SOL   75-65-0 t-BuOH

RX(8)      RCT   Z 358332-98-6

            STAGE(1)
              RGT   M 7664-93-9 H2SO4
              SOL   7732-18-5 Water

            STAGE(2)
              RGT   AB 121-44-8 Et3N, AD 3282-30-2 Pivaloyl chloride
              SOL   109-99-9 THF

            PRO   AC 358332-99-7

RX(17)     RCT   AC 358332-99-7

            STAGE(1)
              RGT   AR 110-18-9 TMEDA
              SOL   109-99-9 THF

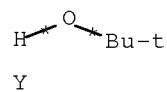
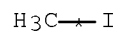
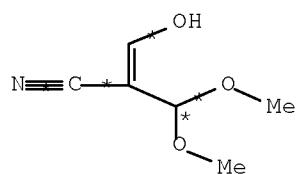
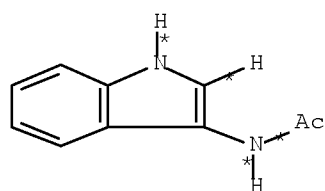
            STAGE(2)
              RGT   AS 594-19-4
              SOL   109-66-0 Pentane

            STAGE(3)
              RGT   AN 109-94-4 HCO2Et

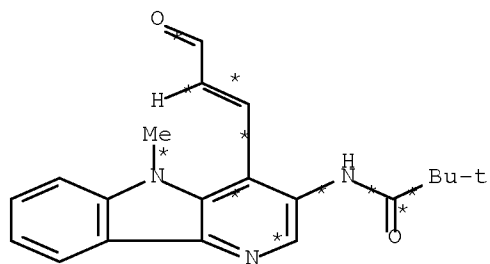
            PRO   AW 358333-10-5
            NTE   stereoselective
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RX(94) OF 95 COMPOSED OF RX(2), RX(3), RX(4), RX(7), RX(8), RX(17)
RX(94)   G + B + H + Y + AS ==> AW
```

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6  
STEPS  
→



YIELD 35%

RX(2) RCT G 51030-59-2, B 105161-33-9

STAGE(1)

RGT D 7647-01-0 HCl

SOL 67-56-1 MeOH, 7732-18-5 Water

STAGE(2)

RCT H 74-88-4

RGT I 7646-69-7 NaH

PRO C 358332-93-1

RX(3) RCT C 358332-93-1

STAGE(1)

RGT K 1310-73-2 NaOH, L 7722-84-1 H<sub>2</sub>O<sub>2</sub>

10/569486

SOL 64-17-5 EtOH, 7732-18-5 Water

STAGE(2)

RGT M 7664-93-9 H2SO4

SOL 7732-18-5 Water

PRO J 358332-94-2

RX(4) RCT J 358332-94-2

STAGE(1)

RGT K 1310-73-2 NaOH

SOL 64-17-5 EtOH

STAGE(2)

RGT D 7647-01-0 HCl

SOL 7732-18-5 Water

PRO O 358332-95-3

RX(7) RCT O 358332-95-3, Y 75-65-0

RGT AA 26386-88-9 (PhO)2P(O)N3, AB 121-44-8 Et3N

PRO Z 358332-98-6

SOL 75-65-0 t-BuOH

RX(8) RCT Z 358332-98-6

STAGE(1)

RGT M 7664-93-9 H2SO4

SOL 7732-18-5 Water

STAGE(2)

RGT AB 121-44-8 Et3N, AD 3282-30-2 Pivaloyl chloride

SOL 109-99-9 THF

PRO AC 358332-99-7

RX(17) RCT AC 358332-99-7

STAGE(1)

RGT AR 110-18-9 TMEDA

SOL 109-99-9 THF

STAGE(2)

RCT AS 594-19-4

SOL 109-66-0 Pentane

STAGE(3)

RGT AN 109-94-4 HCO2Et

PRO AW 358333-10-5

NTE stereoselective

L48 ANSWER 9 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 132:22935 CASREACT Full-text

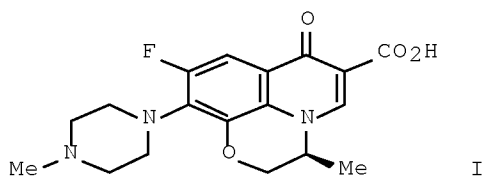
TITLE: A practical stereoselective synthesis of  
(S)-(-)-ofloxacin

AUTHOR(S): Yang, Yu-She; Ji, Ru-Yun; Chen, Kai-Xian

CORPORATE SOURCE: Shanghai Institute of Materia Medica, Chinese Academy

10/569486

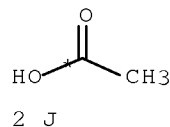
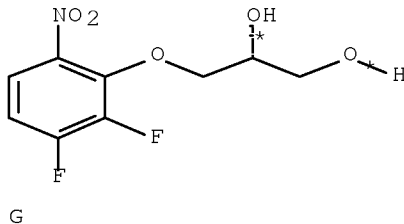
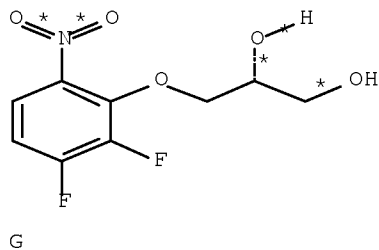
SOURCE: of Sciences, Shanghai, 200031, Peop. Rep. China  
Chinese Journal of Chemistry (1999), 17(5), 539-544  
CODEN: CJOCEV; ISSN: 1001-604X  
PUBLISHER: Science Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI



AB A very efficient and practical procedure for preparation of (S)-(-)-ofloxacin (I) has been developed (10 steps, overall yield  $\geq 45\%$ ). The key step of this approach is the regioselective nucleophilic substitution of 2-position fluorine atom of 2,3,4-trifluoronitrobenzene by (S)-glycerol acetonide.

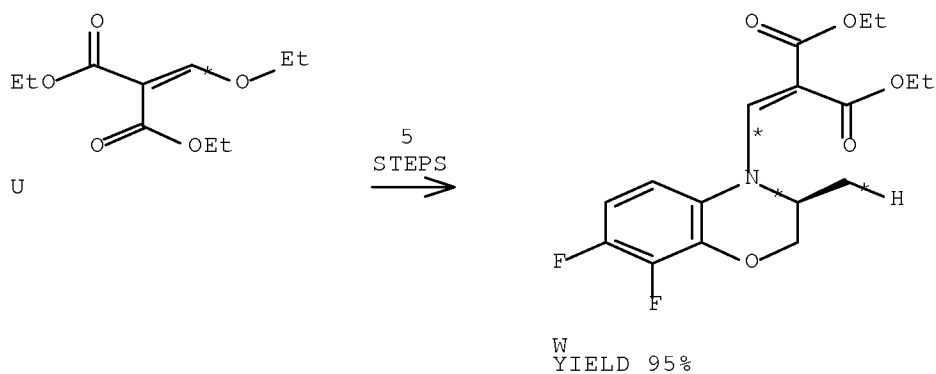
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(38) OF 55 COMPOSED OF RX(3), RX(4), RX(5), RX(6), RX(7)  
RX(38) 2 G + 2 J + U ==> W





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RX(3) RCT G 251945-87-6, J 64-19-7  
RGT M 10035-10-6 HBr  
PRO K 251945-88-7, L 251945-89-8  
NTE 98% overall yield

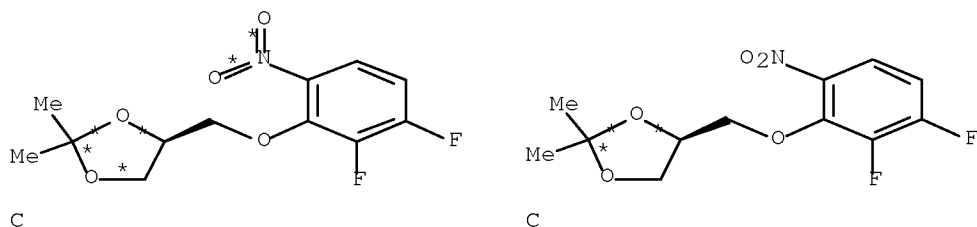
RX(4) RCT K 251945-88-7, L 251945-89-8  
RGT O 1310-73-2 NaOH  
PRO N 132027-28-2  
SOL 7732-18-5 Water  
NTE stereoselective synthesis

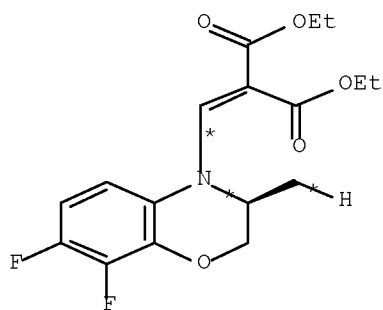
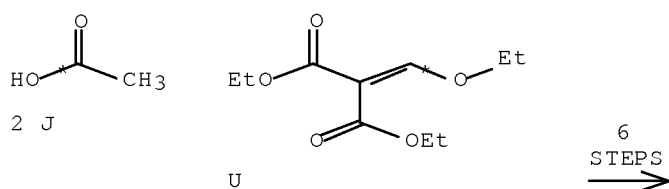
RX(5) RCT N 132027-28-2  
RGT R 1333-74-0 H2  
PRO Q 124409-98-9  
CAT 7440-05-3 Pd, 7440-44-0 Carbon  
SOL 64-17-5 EtOH  
NTE stereoselective synthesis

RX(6) RCT Q 124409-98-9, U 87-13-8  
PRO V 124532-06-5  
NTE heated 145-150

RX(7) RCT V 124532-06-5  
RGT X 1972-28-7 EtO2CN:NCO2Et, Y 603-35-0 PPh3  
PRO W 106939-43-9  
SOL 109-99-9 THF  
NTE stereoselective synthesis

RX(39) OF 55 COMPOSED OF RX(2), RX(3), RX(4), RX(5), RX(6), RX(7)  
RX(39) 2 C + 2 J + U ==> W





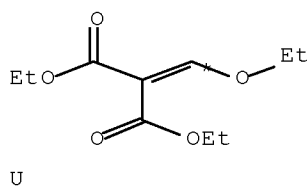
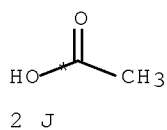
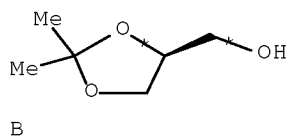
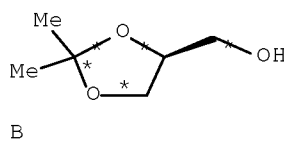
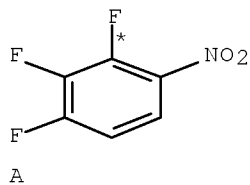
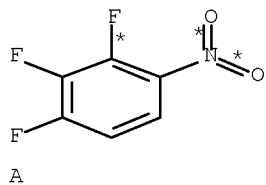
W  
YIELD 95%

RX(2)	RCT	C 251945-86-5
	RGT	H 7647-01-0 HCl
	PRO	G 251945-87-6
	SOL	64-17-5 EtOH
	NTE	stereoselective synthesis
RX(3)	RCT	G 251945-87-6, J 64-19-7
	RGT	M 10035-10-6 HBr
	PRO	K 251945-88-7, L 251945-89-8
	NTE	98% overall yield
RX(4)	RCT	K 251945-88-7, L 251945-89-8
	RGT	O 1310-73-2 NaOH
	PRO	N 132027-28-2
	SOL	7732-18-5 Water
	NTE	stereoselective synthesis
RX(5)	RCT	N 132027-28-2
	RGT	R 1333-74-0 H <sub>2</sub>
	PRO	Q 124409-98-9
	CAT	7440-05-3 Pd, 7440-44-0 Carbon
	SOL	64-17-5 EtOH
	NTE	stereoselective synthesis
RX(6)	RCT	Q 124409-98-9, U 87-13-8
	PRO	V 124532-06-5
	NTE	heated 145-150

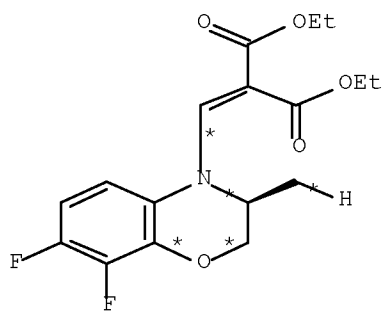
10/569486

RX(7) RCT V 124532-06-5  
 RGT X 1972-28-7 EtO2CN:NCO2Et, Y 603-35-0 PPh3  
 PRO W 106939-43-9  
 SOL 109-99-9 THF  
 NTE stereoselective synthesis

RX(40) OF 55 COMPOSED OF RX(1), RX(2), RX(3), RX(4), RX(5), RX(6), RX(7)  
 RX(40) 2 A + 2 B + 2 J + U ==>  
 W



7  
STEPS  
→



YIELD 95%

RX(1) RCT A 771-69-7

STAGE(1)

RGT D 1310-58-3 KOH, E 584-08-7 K2CO3  
 SOL 108-88-3 PhMe

STAGE(2)  
 RCT B 22323-82-6

PRO C 251945-86-5

RX(2) RCT C 251945-86-5  
 RGT H ~~7647-01-0~~ HCl  
 PRO G 251945-87-6  
 SOL 64-17-5 EtOH  
 NTE stereoselective synthesis

RX(3) RCT G 251945-87-6, J ~~64-19-7~~  
 RGT M ~~10035-10-6~~ HBr  
 PRO K 251945-88-7, L 251945-89-8  
 NTE 98% overall yield

RX(4) RCT K 251945-88-7, L 251945-89-8  
 RGT O 1310-73-2 NaOH  
 PRO N 132027-28-2  
 SOL 7732-18-5 Water  
 NTE stereoselective synthesis

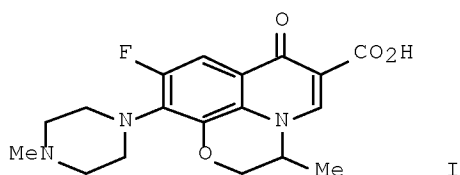
RX(5) RCT N 132027-28-2  
 RGT R 1333-74-0 H2  
 PRO Q 124409-98-9  
 CAT 7440-05-3 Pd, 7440-44-0 Carbon  
 SOL 64-17-5 EtOH  
 NTE stereoselective synthesis

RX(6) RCT Q 124409-98-9, U ~~87-13-8~~  
 PRO V 124532-06-5  
 NTE heated 145-150

RX(7) RCT V 124532-06-5  
 RGT X 1972-28-7 EtO2CN:NCO2Et, Y 603-35-0 PPh3  
 PRO W ~~106939-43-9~~  
 SOL 109-99-9 THF  
 NTE stereoselective synthesis

L48 ANSWER 10 OF 16 CASREACT COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 131:214260 CASREACT Full-text  
 TITLE: An efficient synthesis of ofloxacin and levofloxacin  
 from 3,4-difluoroaniline  
 AUTHOR(S): Adrio, Javier; Carretero, Juan C.; Ruano, Jose L.  
 Garcia; Pallares, Antonio; Vicioso, Mercedes  
 CORPORATE SOURCE: Departamento de Quimica Organica, Facultad de  
 Ciencias, Universidad Autonoma de Madrid, Madrid,  
 28049, Spain  
 SOURCE: Heterocycles (1999), 51(7), 1563-1572  
 CODEN: HTCYAM; ISSN: 0385-5414  
 PUBLISHER: Japan Institute of Heterocyclic Chemistry  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI

10/569486

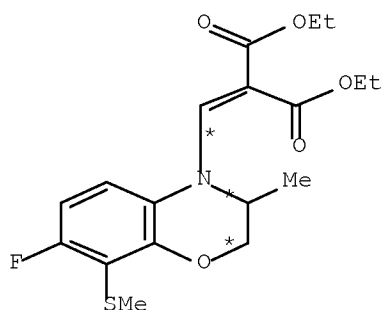
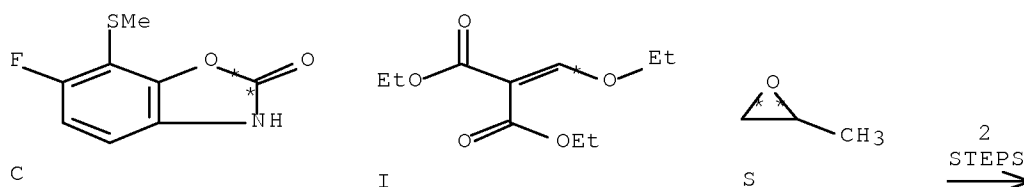


AB The functionalization at either C-2 or C-3 of N-(tert-butoxycarbonyl)-3,4-difluoroaniline, based on its ortho-deprotonation under different exptl. conditions, is described. This process can be readily applied to the synthesis of ofloxacin [(±)-I], levofloxacin [(S)-I], and related compds.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(15) OF 34 COMPOSED OF RX(2), RX(6)

RX(15) C + I + S ==> T



T  
YIELD 41%

RX(2) RCT C 243448-03-5

STAGE(1)

RGT K 1310-58-3 KOH

SOL 7732-18-5 Water, 64-17-5 EtOH

STAGE(2)

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RGT E 7647-01-0 HCl  
SOL 7732-18-5 Water

STAGE(3)  
RCT I 87-13-8

STAGE(4)  
SOL 110-54-3 Hexane

PRO J 243448-07-9  
NTE intermediate adduct was isolated

RX(6) RCT J 243448-07-9

STAGE(1)  
RGT U 7791-03-9 LiClO4  
CAT 7646-69-7 NaH  
SOL 109-99-9 THF

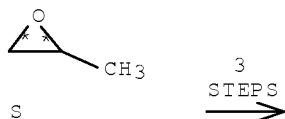
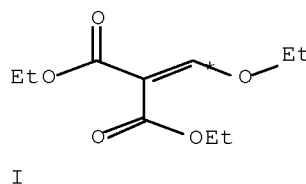
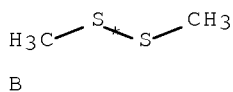
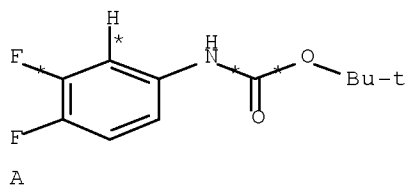
STAGE(2)  
RCT S 75-56-9

STAGE(3)  
RGT H 7732-18-5 Water

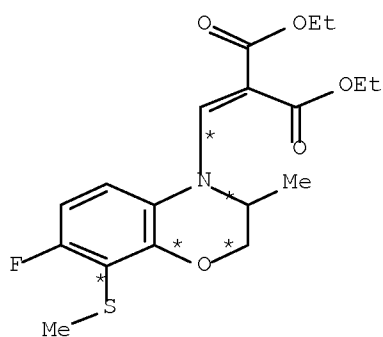
STAGE(4)  
RGT V 603-35-0 PPh3, W 1972-28-7 EtO2CN:NCO2Et  
SOL 109-99-9 THF

PRO T 243448-08-0  
NTE intermediate adduct was isolated

RX(22) OF 34 COMPOSED OF RX(1), RX(2), RX(6)  
RX(22) A + B + I + S ==> T



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T  
YIELD 41%

RX(1) RCT A 144298-04-4

STAGE(1)  
RGT D 594-19-4 t-BuLi  
SOL 109-99-9 THF, 110-54-3 Hexane

STAGE(2)  
RCT B 624-92-0

STAGE(3)  
RGT E 7647-01-0 HCl  
SOL 7732-18-5 Water

PRO C 243448-03-5  
NTE reaction temp. dets. product

RX(2) RCT C 243448-03-5

STAGE(1)  
RGT K 1310-58-3 KOH  
SOL 7732-18-5 Water, 64-17-5 EtOH

STAGE(2)  
RGT E 7647-01-0 HCl  
SOL 7732-18-5 Water

STAGE(3)  
RCT I 87-13-8

STAGE(4)  
SOL 110-54-3 Hexane

PRO J 243448-07-9  
NTE intermediate adduct was isolated

RX(6) RCT J 243448-07-9

STAGE(1)  
RGT U 7791-03-9 LiClO4  
CAT 7646-69-7 NaH  
SOL 109-99-9 THF

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STAGE(2)

RCT S 75-56-9

STAGE(3)

RGT H 7732-18-5 Water

STAGE(4)

RGT V 603-35-0 PPh<sub>3</sub>, W 1972-28-7 EtO<sub>2</sub>CN:NCO<sub>2</sub>Et

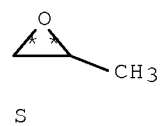
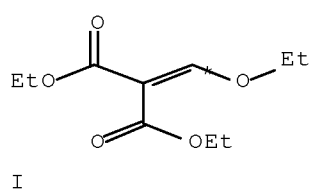
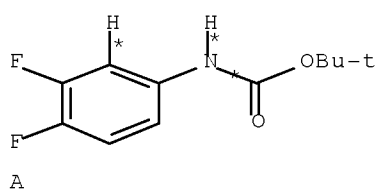
SOL 109-99-9 THF

PRO T 243448-08-0

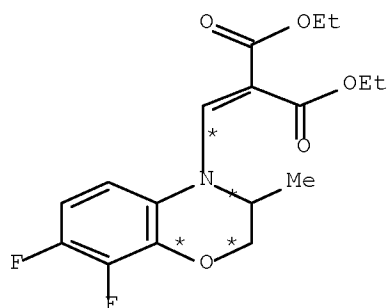
NTE intermediate adduct was isolated

RX(31) OF 34 COMPOSED OF RX(11), RX(10), RX(12)

RX(31) A + I + S ==> AN



3  
STEPS  
→



YIELD 76%

RX(11) RCT A 144298-04-4

STAGE(1)

RGT D 594-19-4 t-BuLi

SOL 109-99-9 THF, 109-66-0 Pentane

STAGE(2)

RGT AK 121-43-7 Me borate

STAGE(3)

RGT AL 7722-84-1 H<sub>2</sub>O<sub>2</sub>

SOL 64-19-7 AcOH, 7732-18-5 Water



STAGE(4)  
RGT E 7647-01-0 HCl

PRO AI 115551-33-2

RX(10) RCT AI 115551-33-2, I 87-13-8  
PRO AJ 85741-74-8  
SOL 64-17-5 EtOH

RX(12) RCT AJ 85741-74-8

STAGE(1)  
RGT U 7791-03-9 LiClO4  
CAT 7646-69-7 NaH  
SOL 109-99-9 THF

STAGE(2)  
RCT S 75-56-9

STAGE(3)  
RGT H 7732-18-5 Water

STAGE(4)  
RGT V 603-35-0 PPh3, W 1972-28-7 EtO2CN:NCO2Et  
SOL 109-99-9 THF

PRO AN 86760-99-8  
NTE S-analog similarly prepd., intermediate adduct was isolated

L48 ANSWER 11 OF 16 CASREACT COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 121:9414 CASREACT Full-text  
TITLE: Process for obtaining benzoxazines useful for the  
synthesis of ofloxacin, levofloxacin and derivatives  
INVENTOR(S): Carretero Gonzalvez, Juan Carlo; Vicioso Sanchez,  
Mercedes; Garcia Ruano, Jose Luis  
PATENT ASSIGNEE(S): Derivados del Etilo, S.A., Spain  
SOURCE: PCT Int. Appl., 30 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Spanish  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9407873	A1	19940414	WO 1993-ES80	19931006
W:	AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN			
RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
ES 2055656	A1	19940816	ES 1992-1983	19921007
ES 2055656	B1	19951116		
ES 2069500	A1	19950501	ES 1993-2080	19931004
ES 2069500	B1	19960301		
AU 9351118	A	19940426	AU 1993-51118	19931006
AU 674542	B2	19970102		
EP 619311	A1	19941012	EP 1993-921930	19931006

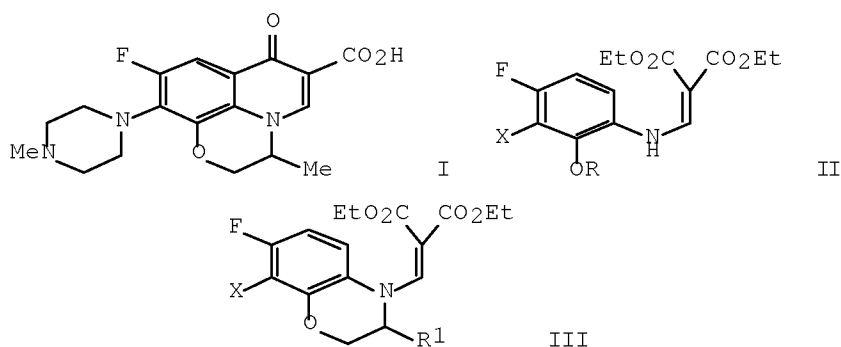
10/569486

R: AT, BE, CH, DE, DK, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

JP 07501835	T	19950223	JP 1993-508738	19931006
KR 131914	B1	19980417	KR 1994-701925	19940607
ZA 9405098	A	19950222	ZA 1994-5098	19940713
US 5521310	A	19960528	US 1994-244455	19940831
AU 9665878	A	19961212	AU 1996-65878	19960927
AU 686955	B2	19980212		

PRIORITY APPLN. INFO.: ES 1992-1983 19921007  
 ES 1993-2080 19931004  
 WO 1993-ES80 19931006

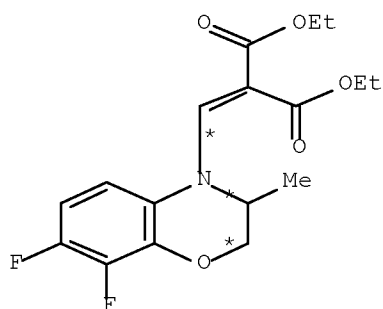
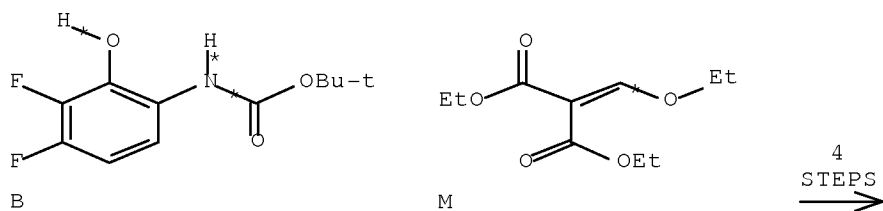
OTHER SOURCE(S): MARPAT 121:9414  
 GI



AB The antimicrobial agents ofloxacin [(±)-I], levofloxacin [(S)-I], and their derivs. and analogs are prepared in several steps. via (anilinomethylene)malonates II [R = H, CH<sub>2</sub>CH(OH)R<sub>1</sub>; R<sub>1</sub> = H, C1-6 alkyl (especially Me), C2-6 alkenyl, aryl; X = halo (especially F)] and benzoxazines III. For example, 3,4-difluoroaniline underwent N-tert-butoxycarbonylation (98-99%), lithiation and hydroxylation in the 2-position (89%), N-deprotection (86%), and condensation with di-Et (ethoxymethylene)malonate (80-81%) to give II [R = H, X = F]. Treatment of this with NaH, LiClO<sub>4</sub>, and propylene oxide in THF gave 65% II [R = CH<sub>2</sub>CH(OH)Me, X = F], which was cyclized by PPh<sub>3</sub> and di-Et azodicarboxylate (79%) to give III [R<sub>1</sub> = Me, X = F]. Cyclization of the latter by AcOH-H<sub>2</sub>SO<sub>4</sub> (73%), saponification by HCl-AcOH (68%), and condensation with N-methylpiperazine (79%) gave (±)-I. By using the appropriate chiral epoxide, and proceeding via enantiomeric intermediates, enantiomeric products such as (S)-I may be obtained without resolution (claimed, no examples).

RX(26) OF 48 COMPOSED OF RX(2), RX(3), RX(4), RX(5)  
 RX(26) B + M ==> R

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YIELD 79%

RX(2) RCT B 155537-32-9  
 RGT K 7647-01-0 HCl  
 PRO J 115551-33-2  
 SOL 60-29-7 Et2O, 7732-18-5 Water  
 NTE room temp.

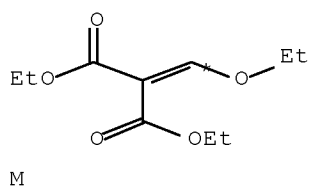
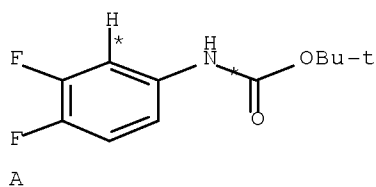
RX(3) RCT J 115551-33-2, M 87-13-8  
 PRO N 85741-74-8  
 NTE neat, 110°

RX(4) RCT N 85741-74-8  
 RGT P 7646-69-7 NaH  
 PRO O 124409-86-5  
 CAT 7791-03-9 LiClO4  
 SOL 109-99-9 THF  
 NTE 40°

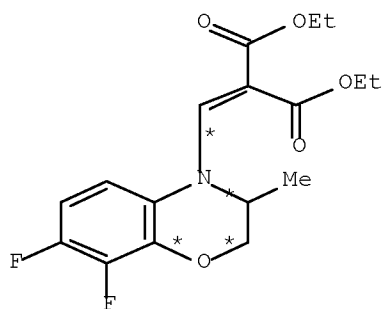
RX(5) RCT O 124409-86-5  
 RGT S 603-35-0 PPh3, T 1972-28-7 EtO2CN:NCO2Et  
 PRO R 86760-99-8  
 SOL 109-99-9 THF  
 NTE room temp.

RX(34) OF 48 COMPOSED OF RX(1), RX(2), RX(3), RX(4), RX(5)  
 RX(34) A + M ==> R

10/569486



5  
STEPS  
→



R  
YIELD 79%

RX(1) RCT A 144298-04-4

STAGE(1)

RGT C 109-72-8 BuLi

SOL 109-99-9 THF, 110-54-3 Hexane

STAGE(2)

RGT D 121-43-7 Me borate

STAGE(3)

RGT E 64-19-7 AcOH, F 7722-84-1 H2O2

SOL 7732-18-5 Water

PRO B 155537-32-9

NTE -78° to room temp.

RX(2)

RCT B 155537-32-9

RGT K 7647-01-0 HCl

PRO J 115551-33-2

SOL 60-29-7 Et2O, 7732-18-5 Water

NTE room temp.

RX(3)

RCT J 115551-33-2, M 87-13-8

PRO N 85741-74-8

NTE neat, 110°

RX(4)

RCT N 85741-74-8

RGT P 7646-69-7 NaH

PRO O 124409-86-5

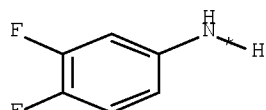
CAT 7791-03-9 LiClO4

10/569486

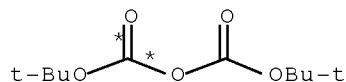
SOL 109-99-9 THF  
NTE 40°

RX(5) RCT O 124409-86-5  
RGT S 603-35-0 PPh3, T 1972-28-7 EtO2CN:NCO2Et  
PRO R ~~86750-99-8~~  
SOL 109-99-9 THF  
NTE room temp.

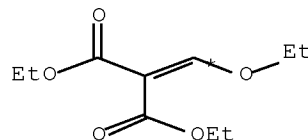
RX(36) OF 48 COMPOSED OF RX(10), RX(1), RX(2), RX(3), RX(4), RX(5)  
RX(36) AE + AF + M ==> R



AE

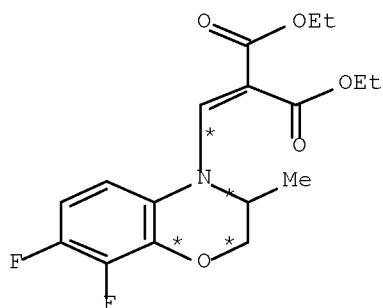


AF



M

6  
STEPS  
→



R  
YIELD 79%

RX(10) RCT AE 3863-11-4, AF 24424-99-5  
PRO A 144298-04-4  
SOL 109-99-9 THF  
NTE 60°

RX(1) RCT A 144298-04-4

STAGE(1)

RGT C 109-72-8 BuLi

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SOL 109-99-9 THF, 110-54-3 Hexane

STAGE(2)

RGT D 121-43-7 Me borate

STAGE(3)

RGT E 64-19-7 AcOH, F 7722-84-1 H2O2

SOL 7732-18-5 Water

PRO B 155537-32-9

NTE -78° to room temp.

RX(2)

RCT B 155537-32-9

RGT K 7647-01-0 HCl

PRO J 115551-33-2

SOL 60-29-7 Et2O, 7732-18-5 Water

NTE room temp.

RX(3)

RCT J 115551-33-2, M 87-13-8

PRO N 85741-74-8

NTE neat, 110°

RX(4)

RCT N 85741-74-8

RGT P 7646-69-7 NaH

PRO O 124409-86-5

CAT 7791-03-9 LiClO4

SOL 109-99-9 THF

NTE 40°

RX(5)

RCT O 124409-86-5

RGT S 603-35-0 PPh3, T 1972-28-7 EtO2CN:NCO2Et

PRO R 86760-99-8

SOL 109-99-9 THF

NTE room temp.

L48 ANSWER 12 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 111:23362 CASREACT Full-text

TITLE: Synthesis of 8,9-difluoro-2-methyl-6-oxo-1,2-dihydropyrrolo[3,2,1-ij]quinoline-5-carboxylic acid

AUTHOR(S): Parikh, Vinod D.; Fray, Andrew H.; Kleinman, Edward F.  
CORPORATE SOURCE: Dep. Med. Chem., Pfizer Cent. Res., Groton, CT, 06340, USA

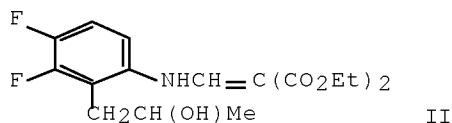
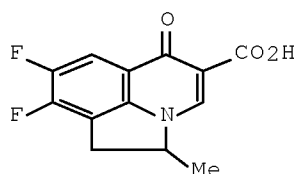
SOURCE: Journal of Heterocyclic Chemistry (1988), 25(5), 1567-9

CODEN: JHTCAD; ISSN: 0022-152X

DOCUMENT TYPE: Journal

LANGUAGE: English

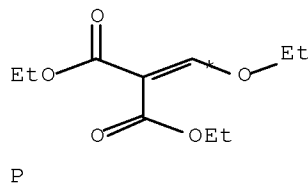
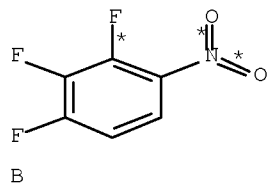
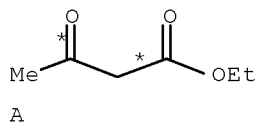
GI



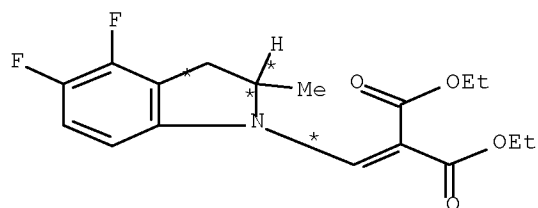
AB The arylation of MeCOCH<sub>2</sub>CO<sub>2</sub>Et by 2,3,4-F<sub>3</sub>C<sub>6</sub>H<sub>2</sub>NO<sub>2</sub> and subsequent hydrolysis-decarboxylation gave 3,4,2-F<sub>2</sub>(MeCOCH<sub>2</sub>)C<sub>6</sub>H<sub>2</sub>NO<sub>2</sub>, which was converted to the title acid (I) via aniline derivative II.

RX(23) OF 28 COMPOSED OF RX(1), RX(2), RX(3), RX(4), RX(5)

RX(23) A + B + P ==> R



5  
STEPS  
→



R  
YIELD 92%

RX(1) RCT A 141-97-9, B 771-69-7

STAGE(1)

RGT D 7646-69-7 NaH

SOL 109-99-9 THF

STAGE(2)

RGT E 7647-01-0 HCl, F 64-19-7 AcOH

SOL 7732-18-5 Water

PRO C 121247-16-3

RX(2) RCT C 121247-16-3  
RGT J 16940-66-2 NaBH<sub>4</sub>  
PRO I 121247-17-4  
SOL 67-56-1 MeOH

RX(3) RCT I 121247-17-4  
RGT M 1333-74-0 H<sub>2</sub>  
PRO L 121247-18-5  
CAT 7440-02-0 Ni

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SOL 64-17-5 EtOH

RX(4) RCT L 121247-18-5, P 87-13-8  
PRO Q 121247-19-6

RX(5) RCT Q 121247-19-6  
RGT S 603-35-0 PPh3, T 1972-28-7 EtO2CN:NCO2Et  
PRO R 121247-20-9  
SOL 109-99-9 THF

L48 ANSWER 13 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 109:190280 CASREACT Full-text

TITLE: Novel quinolone chemotherapeutics. II.  
Thieno[3,2-g]quinoline- and [1]benzothieno[5,6,7-  
ij]quinolizinecarboxylic acids

AUTHOR(S): Sauter, F.; Jordis, U.; Tanyolac, S.; Martinek, P.

CORPORATE SOURCE: Inst. Org. Chem., Tech. Univ. Wien, Vienna, A-1060,  
Austria

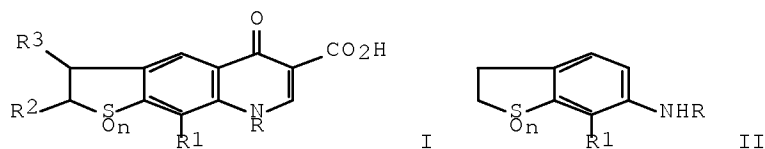
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (1988),  
321(4), 241-6

CODEN: ARPMAS; ISSN: 0365-6233

DOCUMENT TYPE: Journal

LANGUAGE: German

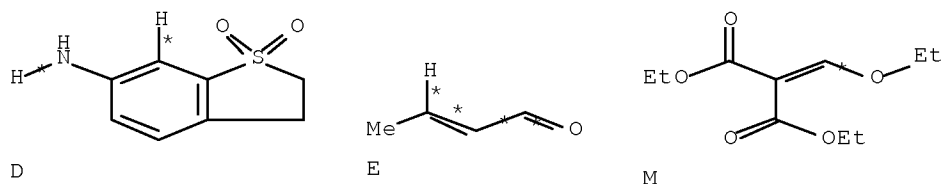
GI



AB The title compds. I [R = H, Et, Me, Ac, R1 = H; RR1 = (CH2)3, CHMeCH2CH2; R2 = R3 = H; n = 0,1,2] were prepared by cyclizing benzothiophenes II with EtOCH:C(CO2Et)2 and ester hydrolysis. In some cases the 2,3-didehydro analogs I(R2R3 = bond) were also obtained. I (RR1 = CHMeCH2CH2, R2R3 = bond) had considerable bactericidal activity against gram-pos. organisms.

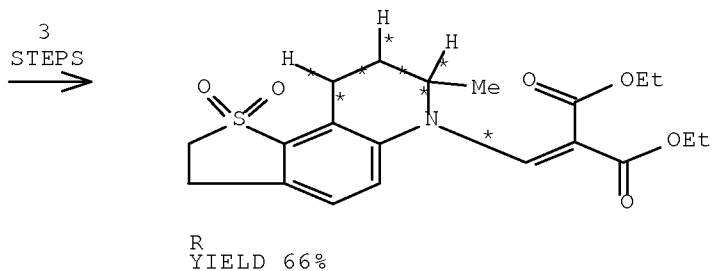
RX(70) OF 125 COMPOSED OF RX(2), RX(3), RX(7)

RX(70) D + E + M ==> R





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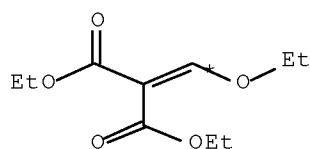
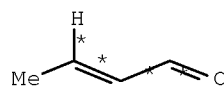
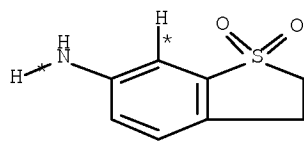
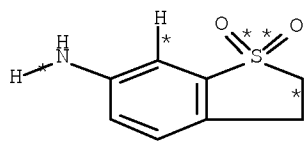
RX(2) RCT D 20503-39-3, E 4170-30-3  
RGT G 7647-01-0 HCl  
PRO F 117080-76-9

RX(3) RCT F 117080-76-9  
RGT I 1333-74-0 H<sub>2</sub>  
PRO H 117080-77-0  
CAT 7440-02-0 Ni  
SOL 108-88-3 PhMe  
NTE Raney Ni

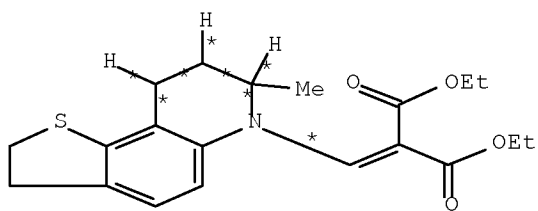
RX(7) RCT H 117080-77-0, M 87-13-8  
PRO R 117080-80-5

RX(77) OF 125 COMPOSED OF RX(2), RX(3), RX(26), RX(11)

RX(77) 2 D + 2 E + M ==> Z



4  
STEPS  
→



YIELD 80%

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RX(2) RCT D 20503-39-3, E 4170-30-3  
 RGT G 7647-01-0 HCl  
 PRO F 117080-76-9

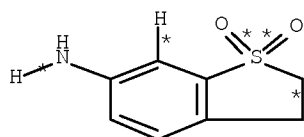
RX(3) RCT F 117080-76-9  
 RGT I 1333-74-0 H2  
 PRO H 117080-77-0  
 CAT 7440-02-0 Ni  
 SOL 108-88-3 PhMe  
 NTE Raney Ni

RX(26) RCT H 117080-77-0  
 RGT AW 1191-15-7 AlH(Bu-i)2  
 PRO Y 117080-98-5, L 117080-99-6  
 SOL 123-91-1 Dioxane

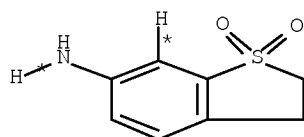
RX(11) RCT Y 117080-98-5, M 87-13-8  
 PRO Z 117080-84-9

RX(79) OF 125 COMPOSED OF RX(2), RX(3), RX(26), RX(12)

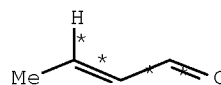
RX(79) 2 D + 2 E + M ==> AA



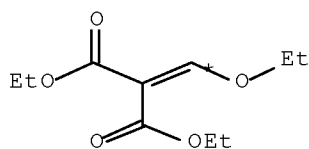
D



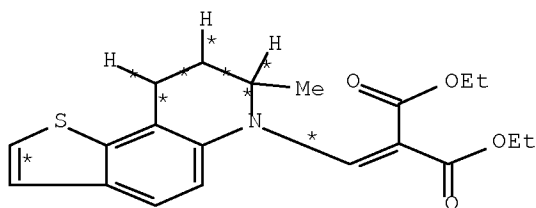
D



2 E



M



AA  
 YIELD 80%

RX(2) RCT D 20503-39-3, E 4170-30-3  
 RGT G 7647-01-0 HCl  
 PRO F 117080-76-9

RX(3) RCT F 117080-76-9  
 RGT I 1333-74-0 H2  
 PRO H 117080-77-0  
 CAT 7440-02-0 Ni  
 SOL 108-88-3 PhMe

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NTE Raney Ni

RX(26) RCT H 117080-77-0  
RGT AW 1191-15-7 AlH(Bu-i)2  
PRO Y 117080-98-5, L 117080-99-6  
SOL 123-91-1 Dioxane

RX(12) RCT L 117080-99-6, M 87-13-8  
PRO AA 117080-85-0

L48 ANSWER 14 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 102:203920 CASREACT Full-text

TITLE: Synthesis of antimicrobial agents. VII. Synthesis  
and antibacterial activities of furo[2,3-g]quinoline  
derivatives

AUTHOR(S): Tanaka, Yoshiaki; Suzuki, Norio; Hayakawa, Isao;  
Suzuki, Kazunori

CORPORATE SOURCE: Res. Inst., Daiichi Seiyaku Co., Ltd., Tokyo, 134,  
Japan

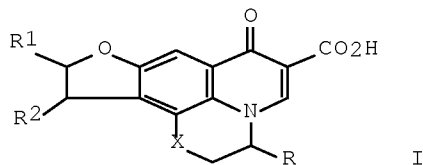
SOURCE: Chemical & Pharmaceutical Bulletin (1984), 32(12),  
4923-8

CODEN: CPBTAL; ISSN: 0009-2363

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

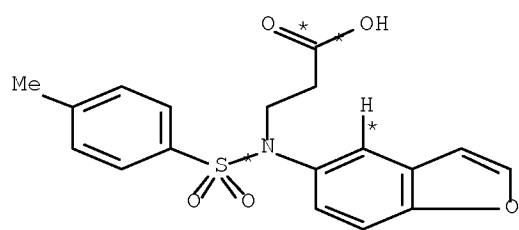


AB Furo[2,3-g]quinolines I (R = H, Me; R1 = R2 = H, R1R2 = bond; X = CH2,O) were synthesized, and their antibacterial activities were examined. Among them, I (R = Me, R1R2 = bond, X = O) exhibited the most potent antibacterial activity against Gram-pos. and -neg. organisms, including *Pseudomonas aeruginosa*, and it showed low acute toxicity to mice.

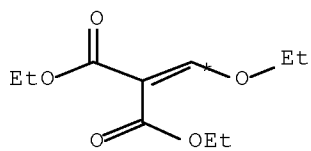
RX(31) OF 49 COMPOSED OF RX(3), RX(4), RX(5)

RX(31) G + L ==> M

10/569486

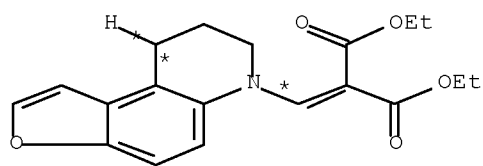


G



L

3  
STEPS  
→



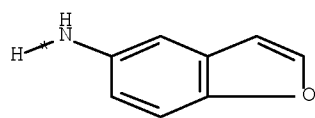
M  
YIELD 55%

RX(3)      RCT    G 73846-19-2  
             RGT    I 10026-13-8 PC15  
             PRO    H 96439-80-4

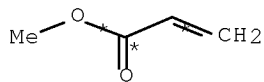
RX(4)      RCT    H 96439-80-4  
             RGT    K 16853-85-3 LiAlH4  
             PRO    J 96439-82-6

RX(5)      RCT    J 96439-82-6, L 87-13-8  
             PRO    M 96439-81-5

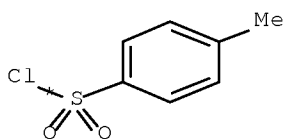
RX(32) OF 49 COMPOSED OF RX(2), RX(3), RX(4), RX(5)  
RX(32)      D + E + F + L ==> M



D

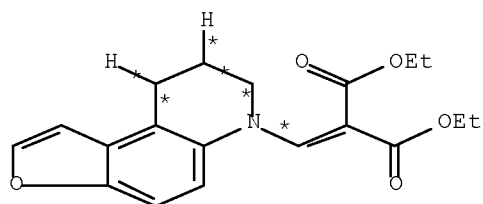
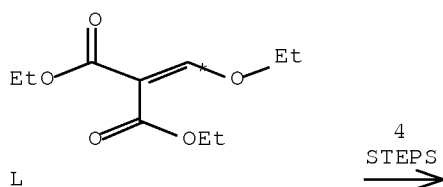


E



F

10/569486



M  
YIELD 55%

RX(2) RCT D 58546-89-7, E 96-33-3, F 98-59-9  
PRO G 73846-19-2

RX(3) RCT G 73846-19-2  
RGT I 10026-13-8 PC15  
PRO H 96439-80-4

RX(4) RCT H 96439-80-4  
RGT K 16853-85-3 LiAlH<sub>4</sub>  
PRO J 96439-82-6

RX(5) RCT J 96439-82-6, L 87-13-8  
PRO M 96439-81-5

L48 ANSWER 15 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 99:138964 CASREACT Full-text

TITLE: Vinyl analog of the Vilsmeier formylation with  
3-(dimethylamino)acroleins

AUTHOR(S): Ullrich, F. W.; Breitmaier, E.

CORPORATE SOURCE: Inst. Org. Chem. Biochem., Univ. Bonn, Bonn, D-5300,  
Fed. Rep. Ger.

SOURCE: Synthesis (1983), (8), 641-5  
CODEN: SYNTBF; ISSN: 0039-7881

DOCUMENT TYPE: Journal

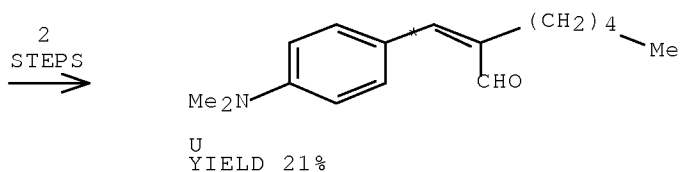
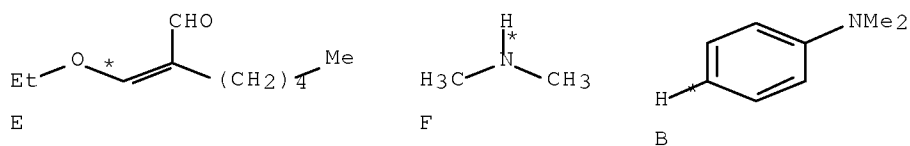
LANGUAGE: German

AB Treatment of PhNMe<sub>2</sub>, pyrrole, or N-methylpyrrole with Me<sub>2</sub>NCH:CRCHO (I; R = H, Me, Et, Pr, pentyl) in the presence POCl<sub>3</sub> gave 13-61% (E)-R<sub>1</sub>CH:CRCHO (R = same, R<sub>1</sub> = p-Me<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>, 2-pyrrolyl or 1-methyl-2-pyrrolyl). The I were prepared by dimethylaminolysis of EtOCH:CRCHO.

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RX(15) OF 22 COMPOSED OF RX(2), RX(11)

RX(15) E + F + B ==> U

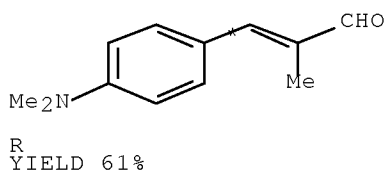
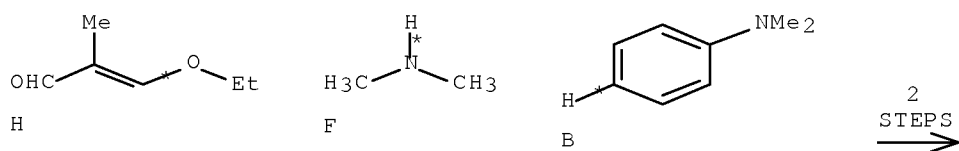


RX(2) RCT E 30989-79-8, F 124-40-3  
 PRO G 57202-65-0

RX(11) RCT G 57202-65-0, B 121-69-7  
 RGT D 10025-87-3 POC13  
 PRO U 344740-58-5

RX(16) OF 22 COMPOSED OF RX(3), RX(8)

RX(16) H + F + B ==> R



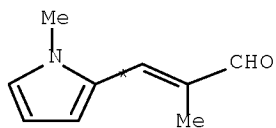
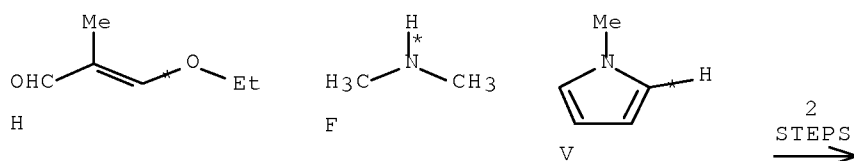
10/569486

RX(3) RCT H 42588-57-8, F 124-40-3  
PRO I 19125-76-9

RX(8) RCT I 19125-76-9, B 121-69-7  
RGT D 10025-87-3 POC13  
PRO R 181381-18-0

RX(17) OF 22 COMPOSED OF RX(3), RX(12)

RX(17) H + F + V ==> W



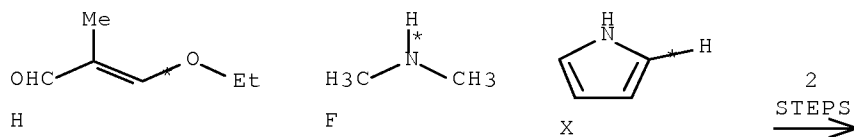
W  
YIELD 13%

RX(3) RCT H 42588-57-8, F 124-40-3  
PRO I 19125-76-9

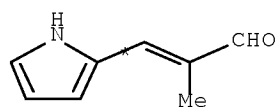
RX(12) RCT I 19125-76-9, V 96-54-8  
RGT D 10025-87-3 POC13  
PRO W 87234-32-0

RX(18) OF 22 COMPOSED OF RX(3), RX(13)

RX(18) H + F + X ==> Y



10/569486

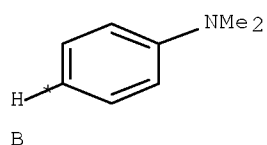
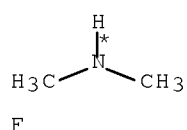
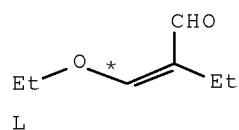


Y  
YIELD 51%

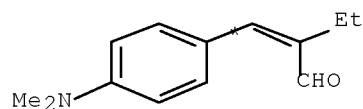
RX(3) RCT H 42588-57-8, F 124-40-3  
PRO I 19125-76-9

RX(13) RCT I 19125-76-9, X 109-97-7  
RGT D 10025-87-3 POC13  
PRO Y 49616-04-8

RX(21) OF 22 COMPOSED OF RX(5), RX(9)  
RX(21) L + F + B ==> S



2  
STEPS  
→



S  
YIELD 37%

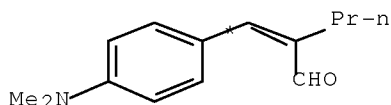
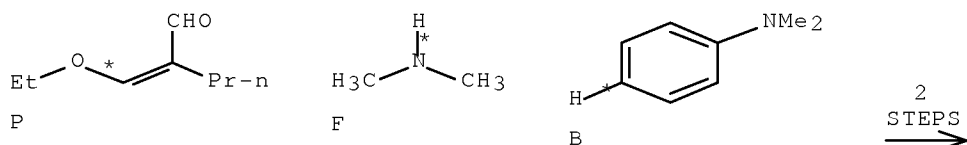
RX(5) RCT L 30989-75-4, F 124-40-3  
PRO M 38062-54-3

RX(9) RCT M 38062-54-3, B 121-69-7  
RGT D 10025-87-3 POC13  
PRO S 87234-34-2

RX(22) OF 22 COMPOSED OF RX(7), RX(10)  
RX(22) P + F + B ==> T



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T  
YIELD 32%

RX(7) RCT P 21037-71-8, F 124-40-3  
PRO Q 87234-37-5

RX(10) RCT Q 87234-37-5, B 121-69-7  
RGT D 10025-87-3 POC13  
PRO T 345640-33-7

L48 ANSWER 16 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 93:239303 CASREACT Full-text

TITLE: Synthesis using allylidenedihydropyridines. VIII.  
Facile preparation of 2-(alkylthio)-3-vinylpyrazolo[1,5-a]pyridines

AUTHOR(S): Kakehi, Akikazu; Ito, Suketaka; Watanabe, Kozo

CORPORATE SOURCE: Fac. Eng., Shinshu Univ., Nagano, 380, Japan

SOURCE: Bulletin of the Chemical Society of Japan (1980),  
53(6), 1775-6

CODEN: BCSJA8; ISSN: 0009-2673

DOCUMENT TYPE: Journal

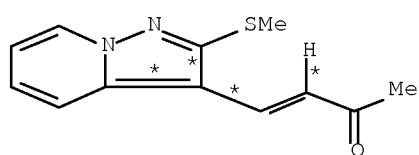
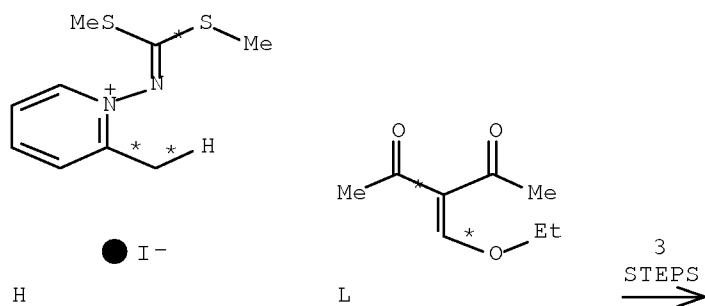
LANGUAGE: English

AB Reactions of 1-[bis(alkylthio)methyleneamino]-2-methylpyridinium iodides with activated ethoxymethylene compds. in the presence of alkali gave the corresponding 1-[bis(alkylthio)methyleneamino]-2-allylidene-1,2-dihydropyridines in considerable yields, and their thermolyses in benzene afforded 2-alkylthio-3-vinylpyrazolo[1,5-a]pyridine derivs.

RX(26) OF 28 COMPOSED OF RX(5), RX(8), RX(10)

RX(26) H + L ==> T

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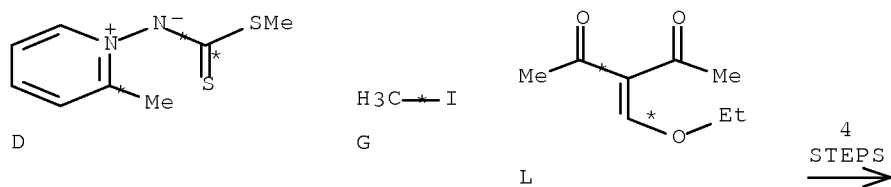
T  
YIELD 65%

RX(5) RCT H 75619-83-9, L 33884-41-2  
PRO M 75619-86-2  
CAT 584-08-7 K<sub>2</sub>CO<sub>3</sub>

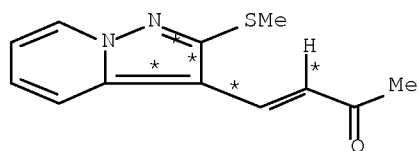
RX(8) RCT M 75619-86-2  
PRO Q 75619-89-5

RX(10) RCT Q 75619-89-5  
RGT U 7647-01-0 HCl  
PRO T 75619-92-0

RX(27) OF 28 COMPOSED OF RX(3), RX(5), RX(8), RX(10)  
RX(27) D + G + L ==> T



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T  
YIELD 65%

RX(3) RCT D 75619-82-8, G 74-88-4  
PRO H 75619-83-9

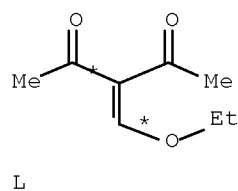
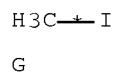
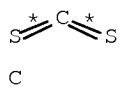
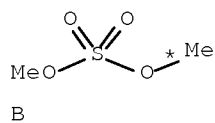
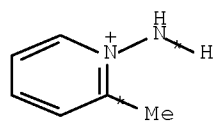
RX(5) RCT H 75619-83-9, L 33884-41-2  
PRO M 75619-86-2  
CAT 584-08-7 K2CO3

RX(8) RCT M 75619-86-2  
PRO Q 75619-89-5

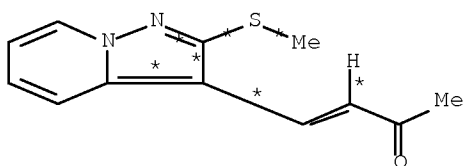
RX(10) RCT Q 75619-89-5  
RGT U 7647-01-0 HCl  
PRO T 75619-92-0

RX(28) OF 28 COMPOSED OF RX(1), RX(3), RX(5), RX(8), RX(10)

RX(28) A + B + C + G + L ==> T



5  
STEPS  
→



T  
YIELD 65%

10/569486

RX(1) RCT A ~~7583-90-6~~, B 77-78-1, C 75-15-0  
PRO D 75619-82-8  
SOL 75-15-0 CS2

RX(3) RCT D 75619-82-8, G 74-88-4  
PRO H 75619-83-9

RX(5) RCT H 75619-83-9, L ~~33884-41-2~~  
PRO M 75619-86-2  
CAT 584-08-7 K2CO3

RX(8) RCT M 75619-86-2  
PRO Q 75619-89-5

RX(10) RCT Q 75619-89-5  
RGT U ~~7647-01-0~~ HCl  
PRO T ~~75619-92-0~~

=> d his full

(FILE 'HOME' ENTERED AT 13:52:54 ON 08 SEP 2008)

FILE 'REGISTRY' ENTERED AT 13:53:56 ON 08 SEP 2008

FILE 'CASREACT' ENTERED AT 13:54:23 ON 08 SEP 2008

ACT BIA486STRL15/A

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L1 STR  
L2 ( 190274)SEA ABB=ON PLU=ON ACYCLIC ALKENE/FG.PRO  
L3 SCR 278 OR 1342  
L4 143 SEA SUB=L2 SSS FUL L1 AND L3 ( 742 REACTIONS)

-----

L5 STRUCTURE UPLOADED  
L6 3 SEA SUB=L4 SSS SAM L5 ( 90 REACTIONS)  
L7 43 SEA SUB=L4 SSS FUL L5 ( 207 REACTIONS)

FILE 'REGISTRY' ENTERED AT 13:56:43 ON 08 SEP 2008

FILE 'CASREACT' ENTERED AT 13:56:57 ON 08 SEP 2008

L8 TRA PLU=ON L4 1- RX : 1312 TERMS

FILE 'REGISTRY' ENTERED AT 13:57:35 ON 08 SEP 2008

L9 1312 SEA ABB=ON PLU=ON L8/RN  
L10 441 SEA ABB=ON PLU=ON L9 AND X/ELS  
L11 421 SEA ABB=ON PLU=ON L10 AND C/ELS  
L12 20 SEA ABB=ON PLU=ON L10 NOT L11

FILE 'CASREACT' ENTERED AT 13:58:10 ON 08 SEP 2008

L13 188275 SEA ABB=ON PLU=ON L12  
L14 24 SEA ABB=ON PLU=ON L13 (L) L7  
L15 48 SEA ABB=ON PLU=ON L13 (L) L4

FILE 'REGISTRY' ENTERED AT 13:59:03 ON 08 SEP 2008

L16 11 SEA ABB=ON PLU=ON L12 AND M/ELS  
L17 9 SEA ABB=ON PLU=ON L12 NOT L16  
D SCA

FILE 'CASREACT' ENTERED AT 13:59:43 ON 08 SEP 2008

L18 153759 SEA ABB=ON PLU=ON L17  
L19 31 SEA ABB=ON PLU=ON L18 (L) L4  
L20 40 SEA ABB=ON PLU=ON L19 OR L14  
L21 15 SEA ABB=ON PLU=ON L19 AND L14  
L22 16 SEA ABB=ON PLU=ON L19 NOT L14  
D OCC  
D OCC 1-16  
D OCC L14 TOT

FILE 'CAPLUS' ENTERED AT 14:03:23 ON 08 SEP 2008

L23 30349 SEA ABB=ON PLU=ON WANG W?/AU  
L24 645 SEA ABB=ON PLU=ON IKEMOTO T?/AU  
L25 8 SEA ABB=ON PLU=ON L23 AND L24

FILE 'MEDLINE, EMBASE, BIOSIS, WPIX' ENTERED AT 14:04:23 ON 08 SEP 2008

L26 9 SEA ABB=ON PLU=ON L25

FILE 'CAPLUS' ENTERED AT 14:04:46 ON 08 SEP 2008

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L27           24 SEA ABB=ON   PLU=ON   L14  
L28           15 SEA ABB=ON   PLU=ON   L21  
L29           16 SEA ABB=ON   PLU=ON   L22  
L30           1 SEA ABB=ON   PLU=ON   (L23 OR L24) AND (L27 OR L28 OR L29)  
L31          143 SEA ABB=ON   PLU=ON   L4  
L32           1 SEA ABB=ON   PLU=ON   L31 AND (L23 OR L24)  
             SEL AN

FILE 'CASREACT' ENTERED AT 14:05:39 ON 08 SEP 2008

L33           1 SEA ABB=ON   PLU=ON   ("143:78029"/AN OR "2005:378843"/AN)  
L34           40 SEA ABB=ON   PLU=ON   L14 OR L21 OR L22  
L35           1 SEA ABB=ON   PLU=ON   L34 AND L33  
             D HIT

FILE 'REGISTRY' ENTERED AT 14:06:39 ON 08 SEP 2008

L36           1 SEA ABB=ON   PLU=ON   ACETIC ACID/CN  
             D RN

FILE 'CASREACT' ENTERED AT 14:06:51 ON 08 SEP 2008

L37          75833 SEA ABB=ON   PLU=ON   64-19-7  
L38           16 SEA ABB=ON   PLU=ON   L37 (L) L4  
L39           14 SEA ABB=ON   PLU=ON   L37 (L) L34  
L40           2 SEA ABB=ON   PLU=ON   L37 (L) L14  
L41           4 SEA ABB=ON   PLU=ON   L37 (L) L21  
L42           10 SEA ABB=ON   PLU=ON   L37 (L) L22  
L43           7 SEA ABB=ON   PLU=ON   L37 (L) L19

FILE 'CAPLUS' ENTERED AT 14:08:44 ON 08 SEP 2008

D STAT QUE L25

FILE 'MEDLINE, EMBASE, BIOSIS, WPIX' ENTERED AT 14:08:55 ON 08 SEP 2008

D STAT QUE L29

FILE 'CAPLUS' ENTERED AT 14:09:16 ON 08 SEP 2008

L44           24 DUP REM L25 L29 (0 DUPLICATES REMOVED)  
             ANSWERS '1-24' FROM FILE CAPLUS

FILE 'REGISTRY' ENTERED AT 14:10:17 ON 08 SEP 2008

FILE 'CAPLUS' ENTERED AT 14:10:19 ON 08 SEP 2008

D STAT QUE L25

FILE 'MEDLINE, EMBASE, BIOSIS, WPIX' ENTERED AT 14:10:32 ON 08 SEP 2008

D STAT QUE L26

FILE 'CAPLUS, EMBASE, WPIX' ENTERED AT 14:10:43 ON 08 SEP 2008

L45           10 DUP REM L25 L26 (7 DUPLICATES REMOVED)  
             ANSWERS '1-8' FROM FILE CAPLUS  
             ANSWERS '9-10' FROM FILE WPIX  
             D IBIB ABS L45 1-8  
             D IALL L45 9-10

FILE 'CASREACT' ENTERED AT 14:11:16 ON 08 SEP 2008

D STAT QUE L14

D STAT QUE L40

D STAT QUE L21

L46           24 SEA ABB=ON   PLU=ON   L14 OR L40 OR L21  
             D IBIB ABS HIT L46 1-24

FILE 'REGISTRY' ENTERED AT 14:17:10 ON 08 SEP 2008

FILE 'CASREACT' ENTERED AT 14:17:14 ON 08 SEP 2008

D STAT QUE L22

D STAT QUE L43

L47 18 SEA ABB=ON PLU=ON L22 OR L43  
 L48 16 SEA ABB=ON PLU=ON L47 NOT L46  
 D IBIB ABS HIT L48 1-16

FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 7 SEP 2008 HIGHEST RN 1047406-12-1

DICTIONARY FILE UPDATES: 7 SEP 2008 HIGHEST RN 1047406-12-1

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<http://www.cas.org/support/stngen/stndoc/properties.html>

FILE CASREACT

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FILE CONTENT:1840 - 31 Aug 2008 VOL 149 ISS 10

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*****
*
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FILE CAPLUS

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FILE COVERS 1907 - 8 Sep 2008 VOL 149 ISS 11  
FILE LAST UPDATED: 7 Sep 2008 (20080907/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/legal/infopolicy.html>

#### FILE MEDLINE

FILE LAST UPDATED: 7 Sep 2008 (20080907/UP). FILE COVERS 1949 TO DATE.

MEDLINE has been updated with the National Library of Medicine's revised 2008 MeSH terms. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

See HELP RANGE before carrying out any RANGE search.

MEDLINE Accession Numbers (ANs) for records from 1950-1977 have been converted from 8 to 10 digits. Searches using an 8 or 10 digit AN will retrieve the same record. The 10-digit ANs can be expanded, searched, and displayed in all records from 1949 to the present.

#### FILE EMBASE

FILE COVERS 1974 TO 8 Sep 2008 (20080908/ED)

EMBASE was reloaded on March 30, 2008.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Beginning January 2008, Elsevier will no longer provide EMTREE codes as part of the EMTREE thesaurus in EMBASE. Please update your current-awareness alerts (SDIs) if they contain EMTREE codes.

For further assistance, please contact your local helpdesk.

#### FILE BIOSIS

FILE COVERS 1926 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT  
FROM JANUARY 1926 TO DATE.



RECORDS LAST ADDED: 3 September 2008 (20080903/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

FILE WPIX

FILE LAST UPDATED: 3 SEP 2008 <20080903/UP>

MOST RECENT UPDATE: 200856 <200856/DW>

DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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>>> IPC Reform backfile reclassifications have been loaded to the end of June 2008. No update date (UP) has been created for the reclassified documents, but they can be identified by 20060101/UPIC and 20061231/UPIC, 20070601/UPIC, 20071001/UPIC, 20071130/UPIC, 20080401/UPIC and 20080701/UPIC. ECLA reclassifications to June and US national classifications to the end of April 2008 have also been loaded. Update dates 20080401 and 20080701/UPEC and /UPNC have been assigned to these. <<<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,  
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[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf)

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE

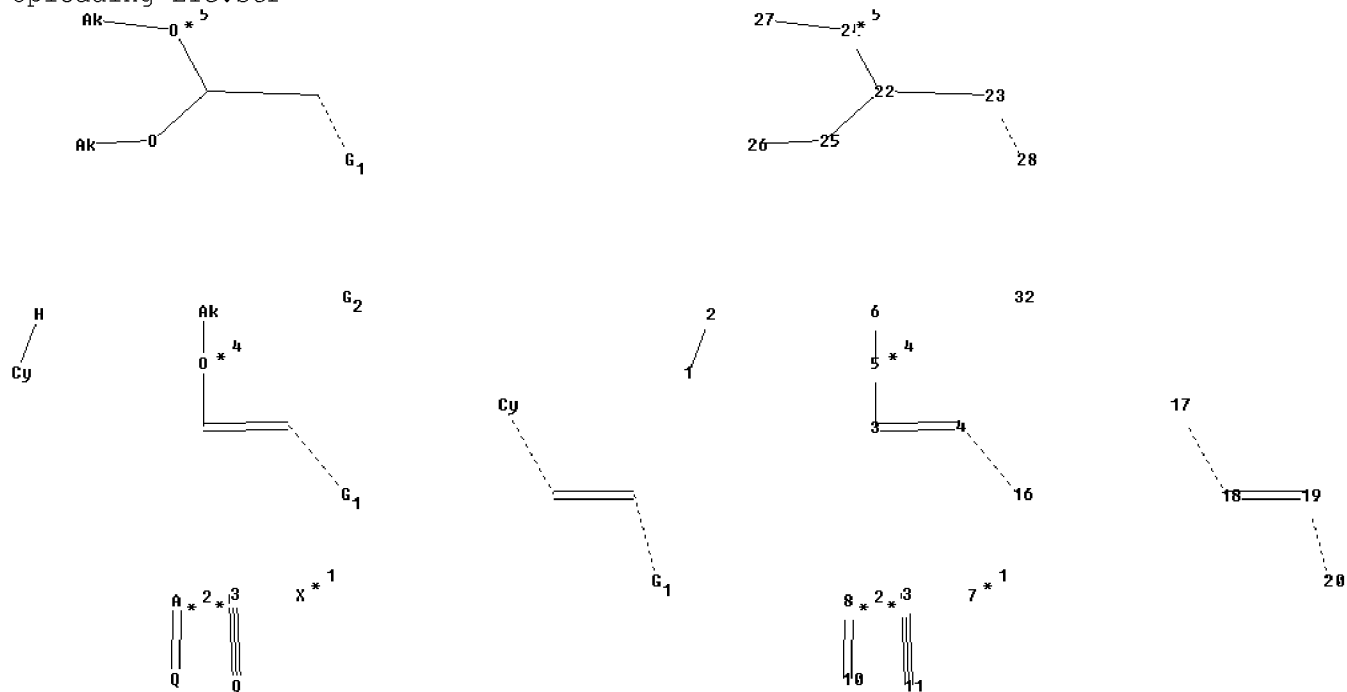
<http://scientific.thomsonreuters.com/support/patents/coverage/latestupdate>

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[http://www.stn-international.com/archive/presentations/DWPIAnaVist2\\_0710.p](http://www.stn-international.com/archive/presentations/DWPIAnaVist2_0710.p)

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

Uploading Llc.str



10/569486

```
chain nodes :
1  2  3  4  5  6  7 16 17 18 19 20 22 23 24 25 26 27 28 32
ring/chain nodes :
8  9 10 11
chain bonds :
1-2  3-4  3-5  4-16  5-6  17-18  18-19  19-20  22-23  22-24  22-25  23-28  24-27
25-26
ring/chain bonds :
8-10  9-11
exact/norm bonds :
1-2  3-5  4-16  5-6  8-10  9-11  17-18  19-20  22-24  22-25  23-28  24-27  25-26

exact bonds :
3-4  18-19  22-23
```

G1:[\*1],[\*2],[\*3]

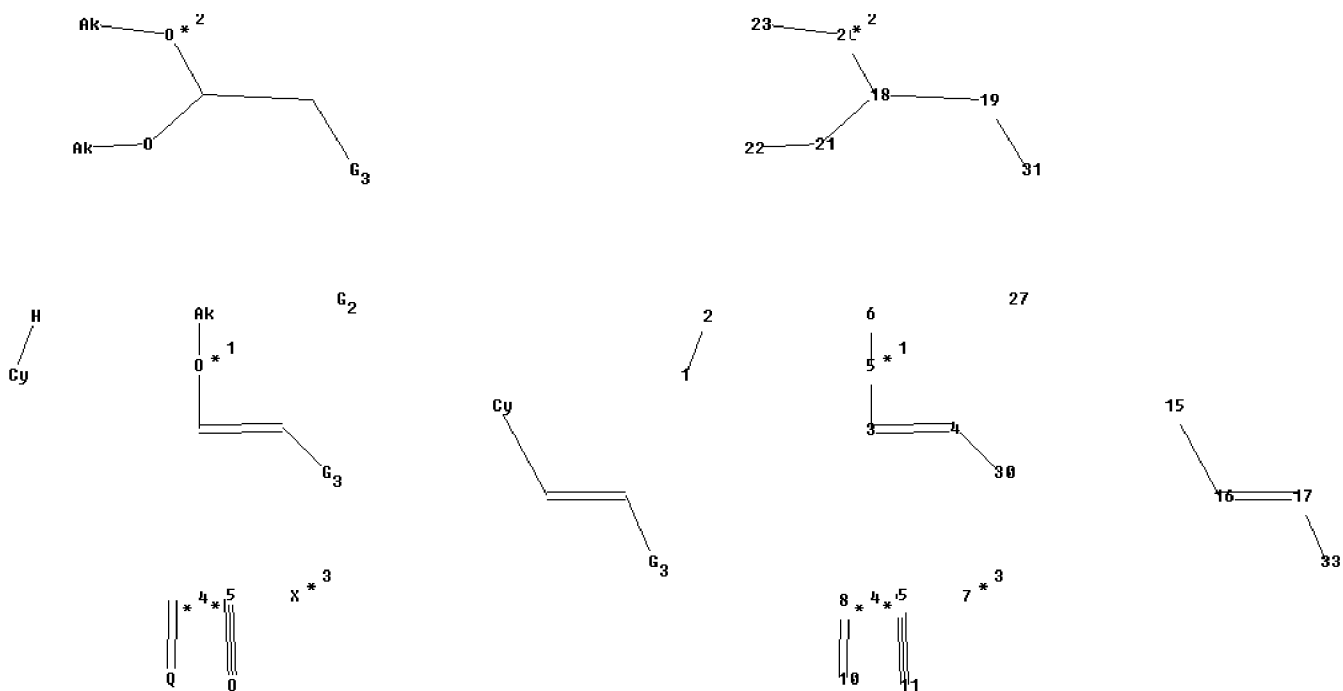
G2:[\*4],[\*5]

```
Match level :
1:Atom  2:CLASS  3:CLASS  4:CLASS  5:CLASS  6:CLASS  7:CLASS  8:CLASS  9:CLASS
10:CLASS
11:CLASS 16:CLASS 17:Atom 18:CLASS 19:CLASS 20:CLASS 22:CLASS 23:CLASS
24:CLASS 25:CLASS
26:CLASS 27:CLASS 28:CLASS 32:CLASS
Generic attributes :
1:
Saturation          : Unsaturated
17:
Saturation          : Unsaturated
```

```
fragments assigned reactant role:
containing 1
containing 32
fragments assigned product role:
containing 17
reaction site bonds:
17-18:CC
```

Uploading L5c.str

10/569486



chain nodes :

1 2 3 4 5 6 7 8 9 10 11 15 16 17 18 19 20 21 22 23 27 30 31  
33

chain bonds :

1-2 3-4 3-5 4-30 5-6 8-10 9-11 15-16 16-17 17-33 18-19 18-20 18-21 19-31  
20-23 21-22

exact/norm bonds :

1-2 3-5 4-30 5-6 8-10 9-11 15-16 17-33 18-20 18-21 19-31 20-23 21-22

exact bonds :

3-4 16-17 18-19

G2:[\*1],[\*2]

G3:[\*3],[\*4],[\*5]

Hydrogen count :

3:= exact 1 4:= exact 1 16:= exact 1 17:= exact 1 18:= exact 1 19:= exact 2

Connectivity :

3:2 E exact RC ring/chain 4:2 E exact RC ring/chain 16:2 E exact RC ring/chain  
17:2 E exact RC ring/chain 18:3 E exact RC ring/chain 19:2 E exact RC ring/chain

Match level :

1:Atom 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS  
10:CLASS  
11:CLASS 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS  
22:CLASS 23:CLASS  
27:CLASS 30:CLASS 31:CLASS 33:CLASS

Generic attributes :

1:  
Saturation : Unsaturated  
15:  
Saturation : Unsaturated

10/569486

fragments assigned reactant role:  
containing 1  
containing 27  
fragments assigned product role:  
containing 15  
reaction site bonds:  
15-16:CC

=>